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PULMONARY FUNCTION STUDIES IN 20 ASTHMATIC PATIENTS IN THE SYMPTOM-FREE INTERVAL

HENRY D. BEALE, B.S., M.D.,* W. S. FOWLER, M.D., AND J. H. COMROE, JR., M.D.

IT IS commonly believed that severe, prolonged, or frequent asthmatic attacks lead to structural changes in the lung that are characteristic of emphysema. We refer to pulmonary emphysema here as that condition associated with breakdown of some alveolar septa, decrease in elastic tissue and diminution in the size of the pulmonary capillary bed. We attempted to determine whether asthma produced such permanent emphysematous alterations by studying pulmonary function in a group of asthmatic patients during symptom-free periods. It soon became apparent that the majority of such patients had abnormal pulmonary function and that, by the tests we employed, we were unable to determine definitively whether the changes in function were due predominantly to airway obstruction or to emphysema. Although the primary objective of the study could not be attained, considerable information was obtained concerning pulmonary function in asthmatic patients.

SUBJECTS

Condensed data upon these are presented in Table I. Twelve female and eight male patients, between the ages of 11 and 66, were studied. The duration of their asthma was from eight months to forty years and the frequency of attacks from one or two per year to one each day. The longest symptom-free period, after the onset of asthma, varied from one day to seven years. Three patients (Nos. 1, 5, and 6) had a history of pneumonia, seven of bronchitis and seven of frequent disease of the upper respiratory tract. The clinical impression of the severity of each patient's asthma was formed on the basis of the frequency,

From the Department of Physiology and Pharmacology, Graduate School of Medicine, University of Pennsylvania and the Allergy Section, Department of Medicine, Hospital of the University of Pennsylvania.

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*Research Fellow of the American Academy of Allergy. Now Instructor in Medicine, School of Medicine, University of Pennsylvania.

TABLE I. CLINICAL AND PHYSICAL DATA

PATIENT	AGE	SEX	HT. (CM.)	WT. (LBS.)	S.A. (M^2)	DURATION OF ASTHMA (YEARS)	LONGEST SYMPTOM-FREE PERIOD	AVERAGE FREQUENCY OF ATTACKS	INTERVAL SINCE LAST ATTACK	SEVERITY OF ASTHMA*
1. E.T.	11	M	146	65	1.12	10	2-3 mo.	3-5 x/yr. Feb.-Aug.	3 wks.	S
2. B.A.	14	M	157	123	1.54	8	6 mo.	1-2 x/wk. May-Sept.	6 mo.	M
3. J.H.	15	F	160	116	1.53	9	7 yrs.	1-2 x/wk. Spring	1 yr.	M
4. A.C.	16	M	166	117	1.58	7	2-3 mo.	Varies 2-3 x/mo.	2 mo.	M
5. L.S.	16	M	179	138	1.78	9	7 yrs.	Daily in some degree	1 day	S
6. S.M.	17	M	183	147	1.86	15	1 day	Daily in some degree	1 day	S
7. D.M.	26	F	161	131	1.62	24	4 yrs.	1-2 x/mo.	1 yr.	M
8. D.R.	30	F	166	134	1.67	⅔	1 day	Daily at night	2 wks.	M
9. V.J.	33	F	161	126	1.59	16	Several months	2-4 x/wk.	2-3 da.	M
10. E.R.	34	F	160	132	1.61	1½	9 mo.	1-3 x/yr. Long dur.	2 wks.	M
11. W.T.	35	M	186	164	1.97	3½	Several months	Varies	Several months	M
12. E.M.	35	F	153	103	1.41	4½	2-3 wks.	Daily 2-3 weeks at a time	2-3 da.	S
13. I.S.	36	F	167	179	1.89	1⅓	1-2 wks.	Varies. Almost nightly	Several days	M
14. J.K.	41	M	168	140	1.71	8	Few days	2-3 x/wk.	1 day	S
15. M.R.	42	F	152	121	1.56	8½	2-3 mo.	2-3 x/wk. 0 in summer	1-2 wks.	M
16. A.J.	42	F	155	133	1.58	6	Several months	2-3 x/winter 1-2 wks. dur.	Several weeks	M
17. R.S.	45	F	152	116	1.48	13	2 mo.	1-2 x/wk. Some daily	Several weeks	S
18. L.L.	50	F	166	144	1.72	40	9 mo.	Daily some degree	1 day	S
19. G.P.	64	F	158	148	1.69	4	1 day	Daily some degree	1 day	S
20. S.F.	66	M	168	122	1.61	30	1 yr.	Daily for one year	Several days	S

*S = Severe; M = Moderately severe.

severity, and length of attacks as well as the duration of the disease. All had at least moderately severe asthma in that they sought medical treatment for their disease most of the time. None of the patients complained of respiratory symptoms at the time of the study. Eighteen were asked to walk on a treadmill at 1.6 miles per hour for four minutes; only patients Nos. 6 and 20 experienced dyspnea during this period. No patient had râles at the time of the study, one (patient No. 14) had wheezes audible on auscultation of the chest and nine had occasional coarse rhonchi. Five of the twelve white patients studied were judged clinically to be mildly cyanotic at the time of the study (Nos. 5, 6, 14, 18, and 20). None of the patients had seasonal asthma at the time of the study. The studies on each patient, before and after bronchiodilator therapy, were done on the same day.

METHODS

All measurements of the lung and ventilatory volumes were made with the subjects semirecumbent except for the maximal breathing capacity (M.B.C.) for which the subjects stood. All volumes were corrected to B.T.P.S.

Vital capacity (V.C.), inspiratory capacity (I.C.; maximal volume that can be inspired from the resting expiratory level) and expiratory reserve volume (maximal volume that can be expired from the resting expiratory level) were determined separately, using a Benedict Roth type spirometer; three trials of each were made and the maximal volume recorded. The spirograms recorded during these tests were examined qualitatively for abnormalities. For the measurement of M.B.C., the subjects breathed for 15 seconds through a mouthpiece, low resistance valve and wide tubing into a carefully counterbalanced compensating recording Tissot spirometer; the maximum of three trials was converted to liters per minute and recorded. Measurements were repeated after administration of either 0.4 c.c. of 0.1 per cent epinephrine subcutaneously or inhalation of 1 per cent epinephrine aerosol.

Residual volume (R.V.) was calculated from functional residual capacity (F.R.C.) which was measured by the open circuit method of Darling.[9] The average difference from the mean of duplicate determinations at the time of this study (1949) was 3 per cent of the F.R.C. Because of the high values obtained, the F.R.C. was calculated on five of the patients by a different method based on analysis of pulmonary nitrogen clearance curves[11]; these values checked within 5 per cent of the values obtained by the Darling method.

Frequency, tidal, and minute volume of respiration during inhalation of air and oxygen were measured by requiring the resting (not basal) subject to breathe through a mouthpiece into the Tissot spirometer.

Two tests of the uniformity of intrapulmonary distribution of inspired gas were performed; these were the single breath and pulmonary emptying rate (P.E.R.)[7] tests. The former was carried out according to the technique of Comroe and Fowler using the Lilly nitrogen and flow meters.[5] The subject expired fully, then inspired oxygen maximally and again expired completely; the rise in N_2 concentration as the subject exhaled 500 ml. of alveolar gas (that between 750 and 1250 c.c. expired gas) was measured. In normal young adults this value does not exceed 1.5 per cent. In the Cournand test for pulmonary emptying rate, the subject after breathing O_2 for seven minutes was required to give a forced expiration; this was sampled continuously by the N_2 meter and the highest value of N_2 was recorded. In normal young subjects, this value does not exceed 2.5 per cent.

Arterial blood samples were analyzed for total O_2 content, O_2 capacity and whole blood CO_2 by the manometric method of Van Slyke and Neill. Blood was rotated with air in a tonometer at room temperature for twenty minutes before measurement of O_2 capacity. Appropriate corrections were made for physically dissolved O_2 and for differences in total hemoglobin in the content and capacity samples to ensure correct calculation of per cent saturation of Hb. Arterial

blood pH was measured in a closed Cambridge glass electrode at 37° C.[4] Plasma CO_2 content and pCO_2 were determined from pH, O_2 capacity and whole blood CO_2, using the nomogram of Van Slyke and Sendroy.[13]

In some subjects, arm-ear and "lung-ear" circulation times were measured using the Millikan oximeter. For the former the initial deflection of the galvanometer following injection of 3 ml. T1824 into an antecubital vein was used as an end point; for the latter the first deflection following the inhalation of O_2 was employed.[10] We also recorded the number of seconds for the oximeter to reach maximal saturation during inhalation of O_2.

Eighteen patients walked on the treadmill at 1.6 miles per hour for four minutes; tidal volume, frequency of respiration and arterial O_2 saturation (oximeter) were recorded during the exercise period and the first five minutes of recovery.

RESULTS

Most of the data obtained are presented in Tables II to IV. Values for circulation times at rest and oximeter readings during and after exercise are not included because they did not vary from normal. The ventilatory volumes

TABLE II. MEASUREMENTS OF LUNG VOLUMES
(ML.)

			VITAL CAPACITY						
PATIENT	I.C.	E.R.	OBSERVED VALUE	% OF PREDICTED VALUE	AFTER EPINEPHRINE	F.R.C.	R.V.	T.C.	$\frac{\text{R.V.}}{\text{T.C.}} \times 100$
1	1130	510	1425	58	--	2650	2140	3565	60
2	2430	1050	3750	95	--	--	--	--	--
3	2150	755	2790	140	--	2065	1310	4100	32
4	2365	1130	3300	80	3760	2340	1210	4510	27
5	3030	1440	4320	97	4480	3930	2490	6810	37
6	2630	920	2800	61	3640	4420	3500	6300	56
7	1635	785	2500	77	--	1900	1115	3615	31
8	2000	920	2730	83	2630	2645	1725	4455	39
9	1715	790	2420	75	2660	2065	1275	3695	35
10	2515	680	3040	95	2930	2535	1855	4895	38
11	3645	1680	5320	114	5370	--	--	--	--
12	1665	555	2270	74	2440	2970	2415	4685	51
13	3080	400	3295	99	--	2480	2080	5375	39
14	2290	860	2380	57	3060	3050	2190	4570	48
15	1680	695	2230	85	2840	3235	2540	4770	53
16	2350	835	3110	111	3030	1975	1140	4250	27
17	1790	760	2375	87	1950	2575	1815	4190	43
18	1125	175	1015	32	1390	1660	1485	2500	59
19	2650	180	1970	96	--	2295	2115	4085	52
20	1360	1425	2480	71	3310	4050	2625	5105	51

I.C. (performed separately) exceeded V.C. in patients 18 and 19, indicating that "air trapping" occurred.

during and after exercise are not included because the great variability of such values in a control group of healthy young adults made it difficult to interpret changes in disease states.

Although there was great variability among individual patients, the majority of the group had a decrease in V.C. and I.C., an increase in F.R.C., R.V.

TABLE III. VENTILATORY MEASUREMENTS

PATIENT	(BREATHING AIR) T.V. (ML.)	(BREATHING AIR) FREQ./MIN.	(BREATHING O_2) T.V. (ML.)	(BREATHING O_2) FREQ./MIN.	M.B.C. (L./MIN.) OBSERVED	M.B.C. (L./MIN.) PREDICTED	M.B.C. (L./MIN.) AFTER EPINEPHRINE	ALVEOLAR GAS UNIFORMITY P.E.R. BEFORE EPI.	ALVEOLAR GAS UNIFORMITY SINGLE BREATH BEFORE EPINEPHRINE	ALVEOLAR GAS UNIFORMITY SINGLE BREATH AFTER EPINEPHRINE
1	400	25	385	17	41	--	47	1.5	6.5	--
2	450	19	470	19	115	122	--	1.0	--	--
3	425	28	385	34	63	98	--	0.7	1.0	--
4	360	29	370	28	96	90	133	1.5	--	0.5
5	655	18	695	17	136	139	163	2.4	4.0	4.0
6	600	16	590	17	62	144	111	4.0	2.5	0.5
7	380	17	425	17	61	124	--	1.0	3.5	--
8	390	19	355	20	105	95	108	1.2	2.0	1.5
9	355	22	355	24	71	89	87	1.0	1.0	1.5
10	450	16	375	17	79	89	93	1.3	2.0	2.0
11	1180	9	910	9	141	135	230	0.8	2.5	2.5
12	370	21	365	23	48	77	46	4.0	4.0	4.5
13	870	12	630	12	99	103	--	1.8	1.0	--
14	465	20	415	21	32	112	62	2.1	6.5	2.5
15	500	20	425	21	56	80	72	2.5	6.0	3.5
16	355	17	465	14	115	81	123	1.2	1.0	1.0
17	350	16	310	17	39	74	39	3.5	3.5	--
18	340	21	350	23	26	82	44	--	3.0*	1.5
19	395	16	345	17	53	69	58	2.7	3.0	--
20	625	18	560	17	34	84	57	6.0	10.0	10.0
Average	495	19.2	459	18.7	74		95			

*Measured at 750-1060 because of small vital capacity.

TABLE IV. ARTERIAL BLOOD STUDIES

PATIENT	% ARTERIAL OXYGEN SATURATION	OXIMETER RATE SECONDS	HEMOGLOBIN GM./100 C.C.	HEMATOCRIT % CELLS	CO_2 CONTENT PLASMA VOLS. %	PCO_2 MM. HG.	pH
1	91.3	--	13.7	--	57.5	43	7.37
2	95.5	50	13.1	41.5	53.4	40	7.37
3	97.8	60	13.4	39	49.1	30.9	7.45
4	98.4	--	13.9	42	54.4	39.5	7.39
5	94.7	90	16.7	52	56.6	31.5	7.51
6	90.5	100	15.9	50.5	58.8	38.1	7.44
7	95.1	--	12.2	39	56.4	42	7.38
8	100.0	--	12.0	44.5	51.4	41	7.37
9	94.1	--	11.8	37	48.0	33.2	7.42
10	95.3	--	11.6	36.5	49.9	34.6	7.41
11	96.2	--	13.0	42	59.2	44	7.38
12	95.0	60	14.1	38.5	55.7	36.5	7.44
13	93.4	30	14.4	40	53.8	35	7.44
14	89.2	240	16.8	50	63.4	42	7.42
15	94.9	--	10.6	34.5	55.8	41	7.38
16	93.8	30	13.3	41	58.8	38	7.44
17	92.0	--	12.4	41	56.2	44.5	7.34
18	86.8	--	13.6	47	56.6	40	7.40
19	91.6	60	13.8	44	53.6	40	7.38
20	91.0	150	14.2	43	53.2	37.5	7.40

and T.C., slight hyperventilation, decrease in M.B.C. (to a greater extent than the V.C.), abnormalities in intrapulmonary distribution of inspired gas, slightly abnormal spirograms, slightly reduced arterial O_2 saturation but normal arterial pCO_2 and pH. The Christie test[3] was definitely positive after maximal inspiration in only three patients, and after maximal expiration in only two.

DISCUSSION

One of the objectives of this study was to obtain more objective evidence upon the relationship between asthma and emphysema. We initially thought that measurements upon asthmatic patients at a time when they were attack-free would reveal emphysematous changes in their lungs; however, certain functional abnormalities were found in practically all of our patients. It then became apparent that it is very difficult to make a sharp differentiation between pulmonary emphysema and asymptomatic, chronic obstructive disease by means of ordinary tests of pulmonary function. In both these conditions, V.C. and I.C. are usually decreased, the R.V. and $\frac{\text{R.V.}}{\text{T.C.}}$ ratio are increased, the M.B.C. reduced to a greater degree than the V.C. and the intrapulmonary distribution of inspired gas is abnormal. In both, the arterial O_2 saturation can be reduced without significant change in arterial pCO_2 or pH. In the case of pure, uncomplicated bronchial asthma, these changes occur because of obstruction to the flow of gas which results in hyperinflation of the lung at its resting expiratory level, reduced velocity of air flow, regional inequalities in distribution of gas and hypoventilation of some areas of the lung. In the case of pure emphysema (uncomplicated by obstruction) these changes occur largely because of reduction in elasticity of the lung which permits the thorax to assume a larger volume at the resting expiratory level, reduces the velocity of air flow especially

in expiration (owing to the lack of assistance in emptying by the elastic recoil) and causes regional inequalities in alveolar ventilation.

Measurements of intrapleural pressure and alveolar pressure in relation to air flow and static pressure-volume relationships should permit differentiation of emphysema and obstructive disease. Techniques for making these measurements were not available to us at the time of this study. Another method which should be capable of differentiating these two diseases would be to determine whether pulmonary function returned to normal values after bronchodilator and antiasthmatic therapy. Baldwin has reported upon a group of asthmatics, in the interval between attacks, who had marked abnormalities in M.B.C. and intrapulmonary distribution of inspired gas.[1] After administration of bronchodilator drugs, the M.B.C. returned to near normal values. This suggests that her patients suffered from reversible obstructive changes and that irreversible structural changes had not developed. Unfortunately in neither our group nor that of Hurtado and Kaltreider[12] was the effect of bronchodilators decisive. Hurtado and Kaltreider studied five asthmatics before and after treatment and found that the R.V. and $\frac{\text{R.V.}}{\text{T.C.}}$ ratio, although improved, were still abnormally high in four of the five; mean values were 2100 c.c. and 40.9 per cent respectively. Six of our patients who received bronchodilator therapy had a V.C. 80 per cent or less of predicted value before treatment; their mean V.C. increased by 18.9 per cent after treatment but returned to predicted values in only one. Eight patients had an M.B.C. 80 per cent or less of predicted values before treatment; their mean M.B.C. increased by 40 per cent but none returned to predicted values after treatment. Alveolar gas uniformity was measured before and after epinephrine in twelve patients; in four it was improved.

To the extent that these changes were reversible by bronchodilator therapy, the pulmonary abnormalities in our patients could be attributed to chronic bronchial obstruction; the changes persisting after therapy could be attributed to irreversible structural alterations, presumably emphysematous in nature. We do not believe that such a conclusion is justified. Bronchial obstruction in chronic asthma may be due to constriction of bronchiolar smooth muscle, to mucosal edema, congestion or secretions and it is possible that more persistent, thorough and varied therapy with bronchodilators (administered both systemically and by aerosol*), chemotherapeutic agents and adrenal cortical hormones is required to restore the normal state.[2]

It was noted that, while none of our patients had dyspnea, many had changes in pulmonary function, especially in M.B.C., of the magnitude that is often associated with dyspnea in patients with emphysema. While we recognize clearly that there is great variability in the level of M.B.C. and breathing reserve at which patients first note dyspnea, we wonder whether dyspnea in patients with emphysema is favored by structural pulmonary damage, which might cause chronic irritation of nerve endings in the lungs.

*Aerosolized bronchodilator agents are directed largely to the better ventilated areas of the lungs and not to the areas of intense bronchial obstruction; the latter areas might be well supplied by the pulmonary and bronchial circulations and hence benefit more from systemically administered bronchodilator drugs.

One of the most important results of the present study has been the finding that asthmatic patients may have definite and marked changes in pulmonary function, at least part of which are due to obstruction, at a time when they are symptom free. The possibilities for harm in long continued bronchial obstruction can only be conjectured. It is possible that localized obstruction can lead to localized infection and result in regional fibrosis or emphysema, and that slight anoxemia may result from hypoventilation of well-circulated alveoli. We did not determine the capacity of these patients for moderate to severe exercise, but we would anticipate that it would be reduced.

It is our opinion that it is desirable to maintain lung volumes and pulmonary function at normal values in the interval between attacks. Toward this end, we would recommend continued, persistent therapy even in the symptom-free interval if necessary. Probably not all asthmatic patients are in need of interval therapy. However, pulmonary function tests offer a means of identifying those patients whose lungs are abnormal between attacks and provide an objective measure of the reversibility of these changes by therapeutic procedures. We believe that testing of pulmonary function during the interval between attacks would be a significant contribution toward evaluation of therapy. It is possible to anticipate only roughly the degree of change in function by the severity of the disease as judged clinically in the sense that the "severe" group had greater changes in pulmonary function (Table V). However, there were patients with definite changes in function even in the "moderately severe" group.

TABLE V

	NUMBER PATIENTS	ART. O_2 SATURATION	$\frac{\text{R.V.}}{\text{T.C.}} \times 100$	ALVEOLAR GAS UNIFORMITY	
				P.E.R.	SINGLE BREATH TEST
Moderately severe	13	95.7	39.4%	1.6	2.4
Severe	7	90.6	52.0%	3.2	5.0

We made no measurements of pressure and flow in the pulmonary circulation or of the uniformity of distribution of the pulmonary blood flow to the alveoli. The studies upon intrapulmonary distribution of alveolar gas, using the N_2 meter, measure only ventilation and not circulation. Decrease in the arterial O_2 saturation indicates that in some patients alveoli were hypoventilated in relation to their pulmonary capillary blood flow but does not identify the cause of the hypoventilation (decreased expansibility, bronchoconstriction, bronchial obstruction, or atelectasis). Baldwin's patients had normal arterial oxygen saturation despite marked abnormalities in the pulmonary nitrogen emptying rate. The latter suggests that some areas of the lung were hypoventilated; the former suggests that these areas received little or no pulmonary capillary blood flow. In our series, only five patients had abnormal P.E.R. and in four of these the arterial O_2 saturation was low. Of fourteen with abnormal distribution as shown by the single breath test, arterial O_2 saturation was low in nine. Our data indicate that at least some hypoventilated areas continue to receive pulmonary blood flow.

There is considerable literature to the effect that patients with bronchial asthma are unduly sensitive to mecholyl or to histamine because these agents produce asthmatic attacks or reduce V.C. in asthmatic patients but not in normal individuals.[8] It is now apparent that many asthmatic patients may have a considerable degree of airway obstruction without reduction in V.C. and without symptoms. Therefore, until further evidence is forthcoming, we believe that the "sensitivity" of asthmatics to mecholyl or histamine can be attributed to the addition of drug-induced bronchial obstruction onto a considerable degree of pre-existing asthmatic obstruction so as to produce a critical state leading to dyspnea and decrease in V.C.

It is of interest to note that all of these patients were able to maintain their maximal rate of breathing over the whole 20 second period of the M.B.C. test. The mean volume breathed in the first 10 seconds did not differ significantly from that in the second 10 second period of the test. This indicates that low values obtained in this test were not due to progressive fatigue of the respiratory muscles. Comroe and associates[6] have suggested that the M.B.C. test serves as a test of fatigability of the respiratory muscles in certain conditions. In patients with myasthenia gravis, a disease characterized by progressive weakness of the affected muscles when undergoing rapid repetitive contraction, the M.B.C. declines with continued effort. A 20 second M.B.C. test may thus serve to differentiate some types of pulmonary disease from conditions characterized by neuromuscular block involving the respiratory muscles.

SUMMARY

Measurements of pulmonary function were made on twelve female and eight male asymptomatic asthmatic patients, 11 to 66 years of age. In general they showed decrease in the vital capacity and inspiratory capacity; an increase in the F.R.C. and in the residual volume, both absolutely and in relation to total capacity; slight hyperventilation; decrease in the M.B.C. (out of proportion to the reduction in V.C.); abnormality in intrapulmonary gas distribution; and slightly abnormal spirograms.

The M.B.C., V.C. and intrapulmonary gas distribution improved following administration of a bronchodilatory drug in many patients indicating that the abnormalities were reversible at least in part and that many asthmatic patients have definite bronchospasm in the absence of signs or symptoms.

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SEROLOGIC INVESTIGATIONS ON THE EDEMA FLUID FROM NASAL POLYPS

A Preliminary Report

Peter Berdal, Oslo, Norway

IT IS well known that there are widely divergent conceptions of the genesis of the usual nasal polyps. Many investigators assume that they are of allergic character, but there is no general agreement about this.

Many authors have regarded the actual development of polyps as a phenomenon of passive congestion, partly due to kinking of the blood vessels (Hajek[3]), partly due to cicatricial changes (Andersen[1]), and partly due to compression in inflammatory processes (Heerup and Kettel,[4] Watson-Williams[6]). Such a passive congestion mechanism seems to be present in some cases. It is hardly probable, however, that this explanation is adequate.

When looked upon on the basis of the extensive histological investigations carried out, for example, by Hansel, Andersen,[1] and many other investigators, it seems scarcely probable in the first instance that the problem can be approached more closely by a morphological examination. I have asked myself whether serological changes are found in the polyp fluid which may contribute to the elucidation of the genesis of the polyps. Considering the many indications pointing to an allergic causation, it is natural to believe that the polyp formation is an expression of an active allergic process, and it would be reasonable then to imagine that this would be reflected in local changes of immunity, demonstrable by serological methods. When a specific antigen enters an allergic nasal or paranasal sinus mucous membrane and brings about an allergic inflammation, it may be assumed that a formation or accumulation of antibodies takes place, which is directed against the allergen in question.

On the basis of this view of the problem I have carried out investigations in a number of patients on the content of antibodies in the polyp fluid and in blood serum. The investigations have been performed in patients who by intracutaneous tests have shown marked reaction to some inhalant or food allergen, and have been carried out by passive transfer of hypersensitiveness by the method of Prausnitz-Küstner and de Besche.[2-5] I have extended the use of this method to comprise also edema fluid from nasal polyps besides blood serum. By parallel investigations of serum and edema fluid from polyps a quantitative comparison has been carried out, between the content of antibodies in edema fluid from polyps and in serum. As basis of comparison has also been used serum from a cantharidin bulla in the patient. The polyp fluid has been procured by squeezing edema fluid from polyps removed under pantocain surface anesthesia. The substrates (polyp fluid, bulla fluid, and serum) have

From the University Hospital, Department of Otolaryngology, Oslo, Norway (Head: Professor Odd Opheim, M.D.).

Kaptein W. Wilhelmsen og Frues Bakteriologiske Institut, Oslo, Norway (Head: Professor Th. Thjøtta, M.D.).

Presented at the 11th Northern Congress of Otolaryngologists, Oslo, June, 1950, and the 3rd Northern Congress of Allergists, Stockholm, June, 1951.

been deposited intracutaneously in the skin on the back of the recipient, and after 24 to 120 hours an extract of the allergen concerned has been injected in the places of deposit of the various substrates. Before the transfer tests have taken place, control of the sterility of the substrates has been carried out and it is a matter of course that the Wassermann reaction of the patient has to be negative.

The quantitative evaluation of the reaction has taken place mostly by a titration of the substrates with a fixed extract dose, but also with fixed substrate dose and titration of the extracts.

I shall give an account of some tests carried out in one patient:

R. T., a 37-year-old housewife, was admitted into the University Hospital, Department of Otolaryngology on Nov. 12, 1948, for nasal polyps. Her mother and her grandmother both had had nasal polyps. She knew of no other case of allergic disease in her family. She had suffered from nasal obstruction for about twenty years. For many years she had also had vasomotor symptoms with sneezing and profuse secretion of mucus. Since 1930 she had been operated on for nasal polyps eight times, the latest time being one and a half years ago. After the third polyp operation in 1935 she developed asthma, which lasted for 6 months (until she got rid of her cat). Her complaints were intensified by tobacco smoke. No further data existed of any special inhalant or food allergen.

TABLE I. (PATIENT R. T.) PASSIVE TRANSFER OF HYPERSENSITIVENESS TO MIXED HOUSE DUST

SUBSTRATE DILUTION	P	B	S	K
1/10	+	+	+	–
1/100	+	(+)	+	
1/250	+	–	(+)	
1/500	+	–	–	
1/1000	+	–	–	
1/2000	+	–	–	
1/4000	(+)	–	–	
1/8000	–	–	–	

Key: P, Polyp fluid. B, Serum from cantharidin bulla. S, Blood serum. K, Controls.

Resection of the septum and bilateral ethmoidal resection had been performed previously. In both nasal cavities were several polyps of medium size with usual appearance and localization. X-ray examination of the paranasal sinuses disclosed swollen mucous membrane in both maxillary sinuses. Leukocytes, 9000; eosinophil cells in the blood, 7.5 per cent; nasal smears, eosinophil cells, +++; intracutaneous allergen tests, hair of dog and cat, +; hair of horse and cow, +++; milk (whole), ++; foxtail grass (Alopecurus pratensis), ++++; timothy, +++; ox-eye daisy, +++; mixed house dust, ++.

Her nasal polyps were removed on Nov. 13, 1948, and from these was squeezed about 1 ml. edematous fluid. The polyp fluid was sterile.

Passive transfer tests were carried out with the polyp fluid, serum from a cantharidin bulla, and blood serum. The substrates in progressive dilution were deposited intracutaneously in the skin on the back of a normal individual, 0.10 ml. in each place of depot. After 24 to 48 hours, 0.025 ml. of extract at a dilution of 1/1000 of one of the allergens to which she reacted positively, was injected intracutaneously in each depot.

A tabular compilation here shows the results of tests with mixed house dust (Table I) foxtail grass (Table II), and milk (Table III).

The result of the test has been that the reaction was positive at the following titers: polyp fluid, 1/2000; bulla fluid, 1/10; serum 1/100. These figures indicate the maximum degree of dilution of each separate substrate in which the reaction is distinctly positive.

TABLE II. (PATIENT R. T.) PASSIVE TRANSFER OF HYPERSENSITIVENESS TO FOXTAIL GRASS

SUBSTRATE DILUTION	P	B	S	K
1/10	+	+	+	–
1/100	+	+	+	
1/250	+	+	+	
1/500	+	+–	+	
1/1,000	+	–	–	
1/2,000	+	–	–	
1/4,000	+	–	–	
1/10,000	+	–	–	
1/20,000	+	–	–	
1/40,000	+	–	–	
1/80,000	+	–	–	
1/160,000	–	–	–	

Result—positive reaction at maximal dilutions—polyp fluid, 1/80,000; bulla fluid, 1/250; serum, 1/500.

By these tests I have recorded, a positive reaction has been found at a far higher titer for polyp fluid than for bulla fluid and blood serum, and furthermore the reaction at the different dilutions is of considerably higher intensity in the polyp fluid than in serum and bulla fluid.

By varying the tests in different ways I have been able to demonstrate that it is a biological phenomenon and not a nonspecific reaction.

In cases of assumed bacterial allergy I have made serological tests with agglutination and complement fixation. It is as yet too early to express any definite opinion on the result of these tests. They seem to point in the same direction, however.

These investigations demonstrate that in some cases of nasal polyps an accumulation is found of specific antibodies against certain definite allergens in the edema fluid of the polyps compared with serum from cantharidin bulla and blood serum. This accumulation of specific antibodies may be assumed to depend upon a local hypersensitiveness.

CONCLUSION

It has been demonstrated that in some cases of nasal polyps an accumulation is found of specific antibodies against certain definite allergens in the edematous polyp fluid as compared with serum from cantharidin bulla and blood serum.

TABLE III. (PATIENT R. T.) PASSIVE TRANSFER OF HYPERSENSITIVENESS TO MILK

SUBSTRATE DILUTION	P	B	S	K
1/1	+	(+)	+	–
1/10	+	–	+	
1/50	+	–	–	
1/100	+	–	–	
1/200	+	–	–	
1/300	+	–	–	
1/500	+	–	–	
1/1,000	(+)	–	–	
1/2,000	–	–	–	

The titers for positive reaction in this case are the following: polyp fluid 1/500, bulla fluid 1/1, serum 1/10.

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HOSPITAL AND AMBULATORY TREATMENT OF ASTHMA AND ECZEMA WITH ACTH AND CORTISONE

HORACE S. BALDWIN, M.D., AND PAUL F. DEGARA, M.D., NEW YORK, N. Y.

THE manifestations of bronchial asthma and of eczema may be initiated by a wide variety of stresses and stimuli.[1] The result has been that the problem of therapy has often resolved itself into the determination and control of the sum total of stimuli, combined with drugs for symptomatic relief. In recent years, moreover, it has become increasingly evident that it is the pattern of tissue response which is fundamentally important.[2] In these diseases the constitutional factor is often inherited, thus making it even more difficult to attempt to change it. The conditions are commonly regarded as allergic, because of the striking role that hypersensitivity may play. Yet, as Wolff and his associates[3] have stated, ". . . It is becoming increasingly clear that the same biologic pattern may be called forth in response to a wide variety of noxious experiences"—not necessarily allergic in origin. Or, as Selye[4] says, "The abnormal adaptive response to the agent is the major cause of the disease." Thus, psychosomatic processes, physical changes, bodily fatigue may be just as important as hypersensitivity factors in calling forth the reaction. With the advent of ACTH and cortisone has come the hope that by their use the fundamental biologic response might be favorably altered to the wide variety of stimuli, which are the active cause of the disease syndrome and the irreversible structural changes which may result.

At the New York Hospital we have been studying the effect of these agents in a series of cases of bronchial asthma and eczema to determine their usefulness in the relief of acute symptoms while hospitalized and following this on an ambulatory basis. Several authors[5] have reported their results in the relief of acute symptoms and relatively short periods of treatment. We also have been interested in this phase of the problem, but further than that we have hoped to determine the scope of usefulness of these drugs when used over a long period of time, their limitations and contraindications and finally to determine eventual changes, if any, in the fundamental constitution of the disease state. Insofar as the longest period of treatment and observation in any of our cases has been eleven months, this is in the nature of a preliminary report.

BRONCHIAL ASTHMA

As will be seen from Table I, the bronchial asthmatic patients (A-1 to A-11) represented a group of intractable cases, for the most part with a wide variety of stimuli and characterized by more or less irreversible structural change. There were 9 men, 2 women, their ages varying from 14 years to 70 years with an average of 49 years. The duration of asthma varied from 2 years to 50 years.

From the New York Hospital-Cornell Medical Center, Departments of Medicine and Pediatrics New York, New York.

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TABLE I. BRONCHIAL ASTHMA
CLASSIFICATION OF CASES

CASE	SEX	AGE	DURATION (YRS.)	EXTRASENSITIVE	SINUS INF'N	PSYCHOSOMATIC	EMPHYSEMA	BRONCHIECTASIS	CARDIAC PULMON.	CORONARY DISEASE
A 1	M	49	40	X	X	X	X			
A 2	M	53	6	0	X		X			
A 3	F	38	23	X	X			X		
A 4	F	45	22	0	X	X	X			
A 5	M	52	31	X	X		X			
A 6	M	55	3	X	X	X				
A 7	M	14	10	X	X	X	X			
A 8	M	50	21	0	X		X			
A 9	M	50	3	0	0			X	X	X
A 10	M	61	2	0	0	X	X			
A 11	M	70	50	X	X				X	X

Extrinsic sensitivities were factors in 6 cases. Chronic nasal sinus infection with or without polypi was present in 9 cases. Psychosomatic causes were considered prominent in 5 patients by psychiatric consultants. Some irreversible changes such as chronic pulmonary emphysema, cardiac pulmonary syndrome and bronchiectases were present in all cases.

Satisfactory symptomatic relief while the patients were treated in the hospital was the general rule (Table II). The average daily dose for each patient while in the hospital varied from 77 mg. to 150 mg. of ACTH or cortisone, and the average daily dose for all patients was 100 mg. Patients A-2, A-5, and A-8 relapsed on ambulatory treatment and had to return to the hospital for more intensive therapy. In none of the patients were there any serious by-effects which could be attributed to either drug.

Nine of the 11 patients were treated on an ambulatory basis following hospitalization (Table III) and 4 of them had satisfactory results. Of the two

TABLE II. BRONCHIAL ASTHMA
SUMMARY OF HOSPITAL TREATMENT

CASE	SEX	AGE	ACTH (GM.)	ACTH DAYS	CORTISONE (GM.)	CORTISONE DAYS	AVERAGE MG. PER DAY	SATISFACTORY RELIEF	DRUG COMPLICATIONS	OTHER COMPLICATIONS
A 1	M	49	0.7	9			77	X	0	0
A 2	M	53	1. 1.4	9	0.2	2	150	X	0	0
			2. 2.3	22			105			
A 3	F	38	1.28	13			100	X	0	0
A 4	F	45	4.16	38			110	X	0	Pneumonia
A 5	M	52	1. 1.52	17	0.2	2	90	X	0	0
			2. 0.99	8			125	X	0	0
A 6	M	55			1.0	10	100	X	0	Coronary spasm
A 7	M	14	1.		0.75	10	75	X	0	0
			2. 0.63	9			70	X	0	0
A 8	M	50	1.		0.85	7	120	X	0	0
			2. 0.64	6			106	X	0	0
A 9	M	50	1.43	16			90	No	0	Myocardial failure
A 10	M	61			0.7	8	106	X	0	0
A 11	M	70			0.85	8	106	X	0	0

patients who failed to continue ambulatory treatment one (A-7) relapsed following his first admission when he returned home to close contact with a dog to which he was sensitive. During his second admission the dog was eliminated and following discharge he has maintained satisfactory relief. The other patient (A-9) who did not continue ambulatory treatment had chronic cardiopulmonary disease and failed to receive symptomatic relief with ACTH while in the hospital. Of the nine patients who received ACTH or cortisone following discharge only 3 have been able to discontinue the use of either drug without relapse.

TABLE III. BRONCHIAL ASTHMA

AMBULATORY TREATMENT

CASE	SEX	AGE	ACTH (GM.)	CORTISONE (GM.)	CORTISONE DAYS	SATISFACTORY	RELIEF WITHOUT ACTH OR CORTISONE	DRUG COMPLICATIONS
A 1	M	49	1.9	2.2	135	Yes	Yes	0
A 2	M	53	0.84	10.8	190	Mod.	No	0
A 3	F	38	2.46		146	Yes	Intermittent	Edema, Acne Hypertension
A 4	F	45	0.38	7.0	206	Mod.	Intermittent	0
A 5	M	52		8.2	210	Mod.	No	0
A 6	M	55		1.4	26	No	No	Depression
A 8	M	50	0.26	1.22	39	No	No	Depression
A 10	M	61		1.0	30	Yes	Yes	0
A 11	M	70		1.0	30	Yes	Yes	0

In four patients with unsatisfactory results, A-2 and A-5 developed severe status asthmaticus while receiving cortisone and had to re-enter the hospital; A-6 following satisfactory hospital care with cortisone when treated on an ambulatory basis with this hormone, had a recurrence of his asthma with marked depression; A-8, after satisfactory hospital management with cortisone, relapsed and on his second hospital admission was controlled with ACTH, only to relapse again while treated ambulatorily, first with ACTH and later with cortisone. Drug complications occurred in 3 of the 9 patients while on ambulatory treatment, depression in 2 of them and temporary hypertension and edema in the third.

ECZEMA

As will be seen from Table IV, the patients with eczema (E-12 to E-19) represented a group of severe cases whose age range varied from 4 months to 75 years. There were 4 males, and 4 females. The duration of eczema varied from 1 month to 19 years. Extrinsic sensitivities were present in 6 patients, chronic infectious foci were demonstrable in 5, and abnormal psychosomatic background was present in 4. Other allergic diseases such as hay fever or asthma were present in 5 of the 8 patients.

In the patients with eczema as with the asthmatics satisfactory symptomatic relief while in the hospital was the rule (Table V). The average daily dose for each patient while in the hospital varied from 36 to 100 mg. of ACTH or cortisone, and the average daily dose for all patients was 70 mg.

TABLE IV. ECZEMA

CLASSIFICATION OF CASES

CASE	SEX	AGE	DURATION	ACUTE	EXTRINSIC SENSITIVITY	CHRONIC INFECT.	PSYCHO-SOMATIC	OTHER ALLERGY
E 12	M	49	15 yr.		X	X	X	Hayfever Asthma
E 13	F	19	19 yr.	1 yr.	X	0	X	Hayfever Asthma Urticaria
E 14	M	16	15 yr.	2½ yr.	X	X	0	Hayfever
E 15	M	75	4 yr.	4 mo.	0	X	0	0
E 16	F	10	8 yr.	4 mo.	X	0	X	0
E 17	M	4 mo.	1 mo.	1 mo.	0	0	0	0
E 18	F	34	14 yr.	5 yr.	X	X	X	Asthma
E 19	F	8	8 yr.	1 yr.	X	X	X	Hayfever

TABLE V. ECZEMA

HOSPITAL SUMMARY

CASE	SEX	AGE	ACTH		CORTISONE		AVERAGE MG. PER DAY	SATIS FACTORY RELIEF	DRUG COMPLI-CATIONS	OTHER COMPLI-CATIONS
			GM.	DAYS	GM.	DAYS				
E 12	M	49	0.7	9			77	X	0	0
E 13	F	19	0.92	25			36	X	0	0
E 14	M	16	1.1	12			92	X	Acne	0
E 15	M	75	0.4	5	0.7	7	90	X	0	0
E 16	F	10	0.3	5			60	X	0	0
E 17	M	4 mo.			0.31	11	28	X	0	0
E 18	F	34	1. 0.9	9	0.3	3	100	X	0	0
			2. 1.13	17			65	X	0	0
E 19	F	8	0.56	11	3.9	62	60	X	0	0

In none of the patients were there any serious complications which could be attributed to either drug.

Five patients were treated on an ambulatory basis following hospitalization (Table VI). Of these, only one has been able to discontinue the use of either drug without serious recurrence.

TABLE VI. ECZEMA

AMBULATORY TREATMENT

CASE	SEX	AGE	ACTH (GM.)	CORTISONE (GM.)	NO. OF DAYS OF TREATMENT	SATIS-FACT.	RELIEF WITHOUT ACTH OR CORTISONE	DRUG COMPLIC.
E 12	M	49	1.9	2.2	135	Yes	Yes	0
E 13	F	19	4.96	0.65	201	Yes	No	Glycosuria
E 14	M	16	1.5	0.5	75	No	Mod.	Acne
E 15	M	75		0.9	21	Mod.	Mod.	Depression
E 18	F	34		5.0	61	Mod.	No	0

Complications attributed to the drugs occurred in 3 cases while being treated on an ambulatory basis. Patient E-13 developed glycosuria during the last 2 to 3 weeks of her treatment. In patient E-14, severe acne occurred. Patient E-15 had temporary depression.

SKIN TEST REACTIVITY

In 10 patients with definite inhalant sensitivity by clinical history and positive skin tests, reactivity to the specific antigens persisted even after prolonged treatment with either ACTH or cortisone and usually as strong as before hormone therapy was started.

ANTIBODY PRODUCTION

The effect of ACTH and cortisone on the production of antibody to typhoid vaccine was studied in 5 patients. Even after prolonged administration of the hormones, antibody production as measured by the agglutination reaction was the same as in two control persons who had not received these substances. These studies are being continued by Dr. Murray Dworetzky and will be reported later.

EOSINOPHILIA

In nonallergic individuals the normal range of eosinophils varies from 80 to 500 per cubic millimeter.[6] In the bronchial asthmatic or in patients with atopic eczema an increase in the severity of symptoms usually results in a definite increase of circulating eosinophils to higher than normal levels. In our series, repeated counts before, during, and after administration of cortical hormone were done on 14 patients, 5 of whom received ACTH, 2 cortisone and 7 both hormones. Eleven of the 14 patients had an increased number of eosinophils prior to treatment and while having active symptoms, ranging from 744 to 2,665 (average, 1419). Although there was a marked initial decrease following ACTH or cortisone treatment, the maximum effect was noted between one and ten days, usually after about 4 days of treatment. At that time approximately 500 mg. of hormones had been given. A drop to zero in circulating eosinophils occurred in only 2 patients, but satisfactory clinical results were noted in all other instances when the level of circulating eosinophils was below the normal, nonallergic range, even when the dosage was reduced. The following is a typical example.

A-5, with pretreatment eosinophil count of 744, was given a daily dose of 100 mg. of ACTH for 11 days. His eosinophils on the 2nd day of treatment had decreased to 47, remained at subnormal levels of 56, 74, and 84 on the fourth, sixth, and eleventh days, respectively, of ACTH therapy. On the twelfth day, the dose of the hormone was reduced to 75 mg., and on the thirteenth day his eosinophils were 328 and remained at the same level for the next 4 days while he received the same daily dose of 65 mg. of ACTH. During this time, however, he was symptom free.

The number of eosinophils increased in 3 other patients at a time when no reduction of hormone dosage had been made but the clinical condition had become more severe.

With the discontinuance of therapy and return of symptoms the eosinophilia tends to return to the abnormally high levels which are comomn in acute asthma and eczema. The following is a typical example.

A-4, on admission with intractable asthma, had an eosinophile count of 2150. Nine days later having received 1320 mg. of ACTH and symptomatically improved, the eosinophil count was 130. During the next 14 days in the hospital she received an additional 1905 mg. of ACTH and was symptomatically much improved; her eosinophil count rose to 452. After her discharge from the hospital she was continued on oral cortisone for about 3 months, receiving a total of 3325 mg. of this hormone. Treatment was discontinued for 4 weeks and her symptoms returned. At this time the eosinophil count was 1054. She was then given 100 mg. of oral cortisone per day. She improved symptomatically and her eosinophil count dropped to 319.

After discontinuation of therapy with ACTH or cortisone eosinophil counts made in 4 patients showed a typical rebound phenomenon.

A number of patients who had received prolonged ambulatory treatment with cortisone had typical eosinopenia following administration of ACTH. The following are examples.

A-2, on his first admission to the hospital, received 1.4 Gm. of ACTH, then 2 Gm. of cortisone on an ambulatory basis. This period comprised 58 days. He relapsed and was admitted in status asthmaticus. At this time, the eosinophil count was 1252. After 240 mg. of ACTH the count was 9. The clinical response was satisfactory.

A-5, on his first admission to the hospital, received ACTH (1.52 Gm.) and then 8.2 Gm. of oral cortisone over a period of 210 days. His asthma recurred and hospitalization was necessary. On admission his eosinophil count was 460. After 40 mg. of ACTH the count was 80 and dropped to 12 in 24 hours after 160 mg. of ACTH. Here again the clinical response was very satisfactory.

The failure to obtain a depression of circulatory eosinophils to zero in 12 of our 14 patients studied could be explained by the increase in the rate of eosinophil production in patients with bronchial asthma and eczema which in these conditions may exceed the peripheral destruction caused by stimulation of adrenal cortical activity.[7, 8] Since the clinical response in these conditions is generally satisfactory if the eosinophil count can be maintained at normal levels, it would seem that while a total depression of circulating eosinophils may be indicated in other conditions,[9] in the allergic diseases the aim should be to maintain them within the levels found in normal nonallergic individuals.

RESPIRATORY FUNCTION TESTS

Complete pulmonary function tests were performed on Patient A-2 (bronchial asthma) by Dr. Daniel S. Lukas of the New York Hospital Cardio-Respiratory Function Laboratory. Before giving ACTH, the vital capacity was restricted and the residual air considerably greater than predicted, comprising 58.4 per cent of the total capacity of the lungs. Maximum breathing capacity was markedly impaired with a low breathing reserve. Following the administration of epinephrine by inhalation the maximum breathing capacity and vital capacity increased. The improvement in pulmonary function measured on the ninth and tenth days of ACTH therapy was striking and much better than that previously produced by inhaled epinephrine. The vital capacity had attained a

normal value, the residual air volume had diminished to normal and now comprised 35.5 per cent of the total capacity. Ventilatory ability was greatly increased, attaining a normal level without administration of additional bronchodilator. Contrary to the result prior to ACTH, the patient did not experience dyspnea during or after the step exercise. Arterial oxygen saturation which before ACTH was definitely low, returned to normal. The patient was then discharged from the hospital and during the next four weeks took an average of 100 mg. of cortisone intramuscularly every other day. At the end of this time his respiratory function tests continued to be normal. His dosage of cortisone was reduced so that in the next 19 days he received only 400 mg. His asthma recurred and he was readmitted to New York Hospital in acute status asthmaticus with marked dyspnea. For three days he was treated with bronchodilators, expectorants, and oxygen without improvement. ACTH was started and within 24 hours he was improved. He was given 1840 mg. of ACTH over the next 14 days and at the end of that time both vital capacity and maximum breathing capacity had returned to normal; a week later he was discharged. For the next 21 days he was given 20 mg. of ACTH twice daily and then 100 mg. of oral cortisone in 4 divided doses per day. Six days later maximum breathing capacity was 98.9 liters per minute or 103.8 per cent of normal predicted value. For the next 21 days he was given 1450 mg. of oral cortisone; then the medication was discontinued. Four days later his maximum breathing capacity was 80.8 liters per minute or 82.7 per cent of predicted normal although subjectively the patient had no complaints. Again, four days later, the maximum breathing capacity had further dropped to 66.8 liters per minute or only 68.4 per cent of predicted normal. At this time it became obvious that the patient was dyspneic and asthmatic. No further respiratory function tests have been carried out since that time.

Thus far, cortisone by inhalation, using a saline solution of Cortisone Acetate (25 mg. per cubic centimeter), has not resulted in relief of bronchial spasm or improvement in respiratory function.

It is our opinion that respiratory function tests, especially the estimation of maximum breathing capacity, offer great aid in proper evaluation of ACTH or cortisone in the treatment of bronchial asthma. It is impossible to tell whether a patient is receiving maximum functional benefit without determining respiratory function variation. Certain patients, especially with pulmonary fibrosis and cardiac pulmonary syndrome, are not likely to be relieved but it is only after careful checking of maximum breathing capacity that a definite conclusion can be drawn.

RHINOLOGICAL RESULTS

The effect of ACTH and cortisone on the nasal membranes is important. The disappearance of nasal polyps under therapy has not occurred in our cases. A-5 was admitted with intractable asthma on Nov. 3, 1950, started on ACTH Nov. 4, received 100 mg. of ACTH daily through Nov. 14, and 75 mg. on Nov. 15 and 16, or a total of 1250 mg., and on Nov. 16 had a nasal polyp removed

surgically. During this period of ACTH therapy, there was no regression of the polyp. A-4 with intractable asthma, a history of bilateral Caldwell-Luc operation in 1948, developed a large nasal polyp which was removed surgically following prolonged treatment with ACTH and cortisone. Treatment with ACTH was started on Sept. 18, 1950, the nasal polyp was removed April 23, 1951, and over this period of time she had received 4.5 Gm. of ACTH and 6.4 Gm. of oral cortisone. A third patient not included in this series, a 42-year-old woman with intractable asthma, had hyperplastic sinusitis with evidence of thickened antral membrane by lipiodol visualization. After daily administration of 100 mg. of oral cortisone for 7 days, there was no evidence of shrinkage of the antral mmebranes. A-1 with asthma was given 700 mg. of ACTH over a period of 9 days but continued to have pale, boggy, nasal membranes with no particular change in appearance according to special rhinological opinion.

On the other hand, A-4 during her initial intensive therapy with ACTH regained her sense of taste and smell which had been completely absent since 1928, after ACTH (3.1 Gm.) was given over a period of 23 days and at the same time rhinological examination showed the "nasal membranes much drier and more atrophic than before ACTH was started." E-7 had hyperplastic lymphoid tissue in her throat with some cervical node enlargement. Under intensive ACTH therapy these tissues regressed to normal appearance. A-7, on admission, had X-ray evidence of a polyp at the base of the left antrum. After 19 days, during which time he received 600 mg. of ACTH and 750 mg. of cortisone, sinus X-rays failed to show evidence of a discrete polyp, although diffuse cloudiness of the left antrum persisted. How much of this disappearance can be attributed to ACTH and cortisone and how much to the change to a hospital environment where he was free from contact with a dog to which he gave positive skin tests, is impossible to tell.

There is no evidence that ACTH or cortisone clear up foci of infection in the nasal sinuses. In three patients with bronchial asthma who had had previously bilateral Caldwell-Luc operations, at times during intensive therapy with either ACTH or cortisone pus could be irrigated from the antra. Careful observations of the nose and throat of other patients during therapy have shown on numerous occasions purulent discharge in the nasal passages.

PSYCHOSOMATIC STUDIES

In diseases so frustrating as intractable bronchial asthma and eczema it is natural that these patients are often greatly disturbed because of the effects of the illness itself on their social and economic life. Suddenly by the administration of ACTH or cortisone they find themselves free of their incubus and able to lead normal active lives. This may result in a feeling of elation almost euphoric. When the dosage is cut or the drug is discontinued and symptoms recur, the patient is naturally disappointed but at the same time has developed a feeling of reassurance that with the return to the drug his symptoms may again be relieved. This feeling of reassurance that ACTH or cortisone will relieve the acute episodes of asthma or eczema serves to remove a great deal of the constant fear of the disease that plagues so many of these patients. As

a result, they may begin to resume their social contacts, return to profitable work, and where deep-seated psychosomatic disturbance is present adapt themselves much better to special psychiatric care. Furthermore, where the constancy of asthmatic attacks has become to a large extent a conditioned reflex the breaking of the reflex arc by long free intervals may exert a very important therapeutic effect. This is particularly true with those who have been using epinephrine sprays or frequent injections of adrenalin for long periods of time, such as A-4. This patient, following the onset of her bronchial asthma 23 years ago, took many hypodermic injections of epinephrine every day until 1940, at which time she collapsed and was ordered to stop the medication. She then resorted to epinephrine by inhalation and used this many times a day until her admission to New York Hospital in September, 1950. It was not until after three weeks of ACTH amounting to a total of 2.5 Gm. had been given that she finally discarded the spray. Thereafter, at times she would have some mild wheezing but adopted the attitude of "not paying too much attention to it," engaging in occupational therapy which she enjoyed. She also adopted a constructive attitude in her conferences with the psychiatrist for solution of her psychosomatic problems which were very profound.

In eczema patients, the constant scratching sometimes seems to be as much a cause of the dermatitis as a result of it. E-2, with eczema since infancy, was finally able with ACTH to stop the scratching which she had done unconsciously. Then, by eliminating her sensitivity factors, instituting immunization and psychiatric care, she definitely improved.

Unfortunately, in some of these patients, particularly those over the age of 50, where the pattern of life has become set, adaptability is less possible, and structural changes in the lungs and cardiovascular system have occurred, the bronchial asthma may quickly return when the dosage of ACTH or cortisone is cut or eliminated. In these patients the physician faces problems caused by the patients' desire to continue therapy over long periods of time, and his own fears of irreparable damage that may result.

The failure of therapy directed solely to the psychosomatic aspects of these conditions had been encountered in several instances. Prior to taking ACTH or cortisone, in at least four patients, two with asthma and two with eczema, thorough efforts with psychotherapy had failed to alter the course of the disease. With these drugs the symptoms were completely relieved, at least temporarily. This would seem to emphasize the point that the constitutional pattern of the disease is not directly approachable through psychoemotional channels alone.

DISCUSSION

It is our impression that ACTH and cortisone represent important advances in the treatment of acute episodes of bronchial asthma and eczema. Satisfactory symptomatic relief while in the hospital was the general rule. In severe status asthmaticus the course was shortened, the intensity of the symptoms ameliorated and the necessity for more drastic procedures, such as intravenous infusions, rectal instillations, inhalations or prolonged sedation and oxygen administration greatly lessened. No serious by-effects were observed when the usual pre-

cautions were taken. On the other hand, it is important to be alert to the masking effects which these drugs may exert on pain and acute intercurrent infection. Patient A-6 (bronchial asthma), a man of 55 years, treated with cortisone intramuscularly toward the end of his hospital stay, had an attack of precordial pain which lasted for about ½ hour. An electrocardiogram taken at that time failed to show any significant change. He left the hospital symptomatically free of asthma and continued injections of cortisone at home until they were discontinued because of signs of mental depression. Asthma recurred and he was readmitted to the hospital where at this time he was treated with the usual remedies but neither ACTH nor cortisone were given. He suddenly died. Autopsy revealed an acute closure of one coronary artery, thus accounting for his death, but also showed another artery with replacement fibrosis that had previously been the seat of a thrombosis. Whether this older lesion occurred on his previous admission coincidental with his precordial pain it is impossible to tell, but it emphasizes the fact that symptoms denoting a serious complication may be masked by these drugs.

A-3, a female, aged 38 years, had asthma complicated by bronchiectases. On three previous admissions for status asthmaticus she had marked apprehension, anoxemia requiring the oxygen tent, antibiotics for the control of infection, and finally ether anesthesia. On her fourth admission she was given ACTH. This time she required no oxygen, very little sedation or bronchodilators. She was calm and assured. After a few days of treatment, however, her pulse rate was 130 per minute, her respiratory rate was 35, numerous râles were present, her sputum was purulent and contained hemolytic streptococcus and Friedlander's bacilli. She was given aureomycin and penicillin; in 24 hours these alarming symptoms disappeared and she made an uneventful recovery. Thus in the treatment of patients with ACTH and cortisone the over-all medical condition must be closely watched. In the presence of hypertension, diabetes, coronary disease and psychopathology these drugs must be used with great caution if at all.

The problem of real importance is to maintain symptomatic relief after the patient leaves the hospital. In patients with intractable bronchial asthma and eczema the symptoms will recur, usually a few days after cessation of the drug. It is therefore important while the patient is hospitalized to survey his sensitivities, foci of infection, psychosomatic factors, and the extent of irreversible structural changes in heart and lungs as well as to take suitable measures to institute immunization or elimination of sensitivities, clear up foci of infection, and improve the psychosomatic status.[10]

In this series we have been particularly interested in the effect of long continued treatment with ACTH and cortisone in patients who continued to have symptoms following discharge from the hospital. Data presented in the foregoing tables indicate that ambulatory treatment with ACTH and cortisone has not been strikingly successful in these intractable cases.

The effective dosage of both drugs on an ambulatory basis varies with the patient. With ACTH 20 mg. twice daily seemed to be the minimum. With

cortisone we have discontinued the intramuscular use because of our impression that the symptoms were better controlled with daily oral medication. In both asthma and eczema the oral dose necessary to control symptoms has been 75 mg. to 100 mg. per day in individual doses of 25 mg. each. Four patients treated with cortisone over long periods improved when given ACTH; this would indicate that these two drugs may be used alternately to solve the problem of patients who need long continued treatment.

It is obvious that ambulatory treatment is determined to some extent by the expense and availability of the drug, the ability of the patient to give himself intramuscular injections of ACTH, the favorable responses of the patient to the drug and complications resulting from its use.

The mechanism responsible for the favorable effects of ACTH and cortisone can only be surmised. Persistence of positive skin tests and conjunctival tests indicate that the fundamental therapeutic effect does not affect the mechanism of sensitization, but may change temporarily the underlying pattern of reactivity. Their use in these conditions has helped to emphasize the basic importance of constitution in these diseases. From a practical clinical standpoint the physician must continue to study the stresses and stimuli in the individual patient which call forth the abnormal constitutional response.

SUMMARY AND CONCLUSIONS

Cortisone and ACTH were used for the treatment of 11 patients with intractable bronchial asthma and of 8 patients with severe atopic eczema. Satisfactory symptomatic relief while the patients were treated in the hospital was the general rule. The necessity for the use of bronchodilators, expectorants, inhalational therapy and sedation was greatly reduced in asthma and for the use of local applications in eczema. Treatment in the hospital varied in duration from 5 to 38 days and required average daily doses of 100 mg. of the hormones for asthma and 70 mg. for eczema.

Ambulatory treatment of 9 patients with asthma and of 5 patients with eczema was continued for periods up to 11 months. During this time as much as 10.8 Gm. of cortisone usually in daily doses of 75 to 100 mg., and 2.5 Gm. of ACTH in amounts of 40 to 80 mg. per day were used. Of the nine asthmatics who received ACTH or cortisone following discharge from the hospital only 3 have been able to discontinue the use of either drug without relapse and of the 5 patients with eczema only one has been able to discontinue these drugs without recurrence. Although several patients received hormone therapy for many months, none experienced serious side effects. It should be pointed out, however, that all of them were kept under constant and careful medical supervision.

Skin test reactivity persisted after prolonged treatment with either ACTH or cortisone.

Antibody production to typhoid vaccine as measured by the agglutination reaction was studied in 5 patients. After prolonged treatment with ACTH and cortisone the agglutination titers were the same as in the controls.

With ACTH and cortisone satisfactory clinical response in bronchial asthma and eczema was associated with reduction of the eosinophil count to levels found in normal nonallergic individuals.

Respiratory function tests, especially the estimation of maximum breathing capacity, are essential to determine whether the patient with bronchial asthma is receiving maximum functional benefit from ACTH and cortisone.

In spite of prolonged administration of ACTH and cortisone nasal polyps may persist and there is no evidence that these hormones clear up foci of infection in the nasal sinuses.

ACTH and cortisone generally improve the attitude of patients with asthma and eczema to their disease. The failure of therapy directed solely to the psychosomatic aspects of these conditions contrasted with the improvement manifested with ACTH and cortisone indicates that the constitutional pattern of the disease is not directly approachable through psychosomatic channels alone.

The danger arising from the masking effect of ACTH and cortisone on pain and intercurrent infection is indicated.

The importance of studies of the stresses and stimuli in the individual patient responsible for the abnormal constitutional response is emphasized.

The mechanism responsible for the favorable effects of ACTH and cortisone in bronchial asthma and eczema is unknown. It is suggested that the fundamental therapeutic effect is to change temporarily the underlying pattern of constitutional reactivity.

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CLINICAL STUDIES WITH CORTISONE BY MOUTH, CORTISONE BY INJECTION, AND ACTH IN THE TREATMENT OF ASTHMA

WILLIAM FRANKLIN, M.D., FRANCIS C. LOWELL, M.D., IRVING W. SCHILLER, M.D., AND HENRY D. BEALE, M.D.

THIS report summarizes our experience over a period extending from December 1949 to January 1951 with ACTH and cortisone in the treatment of bronchial asthma*

Twenty-five asthmatic patients received ACTH and cortisone by injection (subcutaneously or intramuscularly) and cortisone by mouth. Most of the patients received several courses of treatment and some received each of the three agents at least once. As may be seen in Table I, there were 25 courses

TABLE I

DRUG	CASES	COURSES
Cortisone I.M.	11	25
Cortisone P.O.	14	22
ACTH	16	23
Total	25	70

of cortisone by injection in 11 patients, 22 of cortisone by mouth in 14, and 23 of ACTH in 16, or a total of 70 courses in 25 patients. All of the patients had severe asthma and had been hospitalized at least once in the recent past for this reason. Twelve patients who received the first course of ACTH or cortisone in the hospital had failed to respond to intensive treatment which included intravenous aminophylline and epinephrine. Three patients were on the danger list and 2 of these had clear-cut respiratory acidosis and are discussed elsewhere.[1] Thirteen patients were treated as outpatients, although in most instances had ACTH and cortisone been unavailable, they would have required hospitalization.

Although dosage varied, most patients were treated with 80 mg. of ACTH or 100 to 300 mg. of cortisone daily, until marked or maximum improvement occurred. Improvement was judged by statements made by the patient, the need for other medication, vital capacity and expiratory rate, and, in some instances, maximum breathing capacity, residual air, the uniformity of pulmonary mixing,[2] and the arterial oxygen saturation, pH and CO_2 content. The weight, blood pressure and total eosinophil count were followed in every case.

From the Allergy Clinic, Evans Memorial, Massachusetts Memorial Hospitals and the Department of Medicine, Boston University School of Medicine, Boston, Massachusetts.

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Of the 25 cases there was complete temporary relief of symptoms in 17, with return to full activity and elimination of the need for other medication. Six patients, though markedly improved and able to resume normal activity in large part, continued to have symptoms and continued to use bronchodilator drugs despite intensive treatment with ACTH or cortisone. Two patients, both elderly women, improved markedly, but are difficult to assess because they were bedridden for other causes. Finally, ACTH seemed to be entirely ineffective in two patients who received 3 courses as follows: 80 mg. daily for 11 days followed by 120 mg. daily for 3 days; 80 mg. daily for 7 days. Not only was there no improvement in the asthma, but there was likewise no fall in the eosinophil count. ACTH was not given intravenously to these patients. Both patients also received courses of cortisone in a dose of 200 mg. daily for 7 and 22 days, respectively, and in each instance there was complete clearing of symptoms. However, there was again no fall in the eosinophil count within the first 24 or 48 hours of treatment as occurred with regularity in the other patients. The time required for initial improvement, maximum improvement, and relapse, irrespective of dose, is shown in Tables II, III, and IV. In general, initial

TABLE II

INITIAL IMPROVEMENT

DRUG	COURSES EVALUATED	NUMBER OF CASES SHOWING INITIAL IMPROVEMENT IN HOURS <12	HOURS 12-24	DAYS 1	DAYS 2	DAYS 3-5	DAYS >5	MEDIAN TIME
ACTH	12	1	2	7	1	1		1
Cortisone I.M.	17			1	5	7	4	3
Cortisone P.O.	17	1	3	8	2	2	1	1

TABLE III

MAXIMUM IMPROVEMENT

DRUG	COURSES EVALUATED	NUMBER OF CASES SHOWING MAXIMUM IMPROVEMENT IN DAYS 2-3	4-7	8-14	15-21	>21	MEDIAN TIME
ACTH	14		7	6	1		8
Cortisone I.M.	10			4	6		15
Cortisone P.O.	18	2	3	8	2	3	10

TABLE IV

RELAPSE

DRUG	COURSES EVALUATED	DAYS FOR RELAPSE-NUMBER OF CASES <1	1-3	4-7	8-14	15-30	31-60	>60	MEDIAN TIME
ACTH	13	5	2		2	2	1	1	4
Cortisone I.M.	11		2	3	5	1			8
Cortisone P.O.	12	2	3	2	3	1	1		7

improvement was apparent earlier when cortisone by mouth or ACTH was given, as compared with cortisone by injection. One half of the patients receiving cortisone by mouth or ACTH improved within one day, whereas the time required was 3 days for those receiving cortisone by injection. Indeed, 3 pa-

tients receiving ACTH and 4 receiving cortisone by mouth showed improvement in less than 24 hours. Table III shows the time required for maximum improvement and shows a similar pattern. In the foregoing, dosage was omitted from consideration, but, in general, the larger doses produced more rapid improvement.

Table IV shows the time required for the reappearance of symptoms after treatment was stopped. In five patients receiving ACTH relapse began within 24 hours of the last dose, and the same was true for two patients receiving cortisone by mouth. In the case of injectable cortisone, not only was the initial effect delayed as mentioned above, but relapse within 24 hours after treatment was stopped did not occur. In general, half of the patients relapsed within about one week. The duration of remission did not seem to depend on the intensity or duration of treatment. The time required for relapse varied from patient to patient and at different periods in the same patient. Relapse was sometimes delayed long after the systemic effects of treatment had passed as indicated by a return of the eosinophil count to the initial level and disappearance of side effects when present. Three patients developed mild symptoms after treatment was stopped, which cleared or did not increase in spite of witholding further treatment with ACTH or cortisone. In the entire group there have been only 7 remissions (two in one patient) of 15 days or longer.

Although there were certain exceptions, the smallest effective dose of cortisone (injectable or oral) was approximately 100 mg. daily and of ACTH approximately 40 mg. daily. Smaller doses frequently failed to cause improvement or prevent relapse, and the minimum dose required varied not only from patient to patient but from time to time in the same patient. When relapse did not occur with small doses, it was often difficult to know whether this was a consequence of continued treatment with small doses or whether the patient would do equally well with no treatment.

Prolonged treatment with ACTH or cortisone in certain patients with severe chronic bronchial asthma raises a number of questions which will require time to answer. Our limited experience to date has been encouraging. Ten patients have received cortisone or ACTH intermittently or almost continuously for three months or more as shown in Table V. Seven patients received one or the other agent more than half of the time. In all ten patients disability from asthma was markedly reduced and the vital capacity increased, greatly so in five, and the expiratory rate became more rapid. The beneficial effects of treatment on anoxia and respiratory acidosis in the first patient in Table V is described elsewhere.[1] The capacity for effort was increased in all patients. Two patients (Nos. 1 and 3 in Table V), for whom treatment was clearly lifesaving, were able to engage in full-time employment as long as treatment was continued, and one patient (No. 4, Table V), who had been a pulmonary cripple since early childhood, was likewise able to engage in sedentary employment for the first time. In spite of the marked improvement just described, these patients continued to use some ancillary medication, and this was true of most of the remaining patients in whom mild symptoms of asthma often persisted during treatment with ACTH or cortisone in the dosage used.

TABLE V. CASES TREATED OVER A PERIOD OF THREE MONTHS OR LONGER

PATIENT	DURATION OF SYMPTOMS (YEARS)	TOTAL TIME 1ST DOSE TO 1/1/51	DAYS ACTUALLY RECEIVING DRUG	% TIME TREATED	COURSES	GRAMS			% DISABILITY		VITAL CAPACITY	
						ACTH	CORTISONE I.M.	CORTISONE P.O.	BEFORE	AFTER	BEFORE	AFTER
1. RK 54 M	10 mo.	403	339	84	5	7.21	15.23	5.15	100	10	1200	5000
2. MK 54 F	6	339	251	74	7	2.63	6.48	10.40	100	0	1300	3000
3. EC 49 M	6	310	288	93	6	6.83	11.70	17.20	100	15	1700	3750
4. RD 21 M	20	270	220	81	7	5.46	4.85	23.80	80	20	1700	2800
5. DS 52 F	8	264	124	47	7	2.12	8.02	2.30	80	0	1500	2700
6. LD 19 M	17	206	143	69	5	2.88	3.15	3.75	30	0	2200	4100
7. FD 9 M	9	108	100	93	?	--	0.35	10.30	60	0	1550	2050
8. GJ 65 M	20	107	59	55	3	--	0.60	9.95	70	0	2200	3000
9. HH 53 F	4	107	42	39	3	--	0.55	2.80	60	0	1600	2150
10. MC 44 F	8	92	17	19	2	0.10	2.40	0.40	100	0	1850	3300

The only serious side effects noted were not attributable to prolonged treatment. One patient, not included in Table IV, developed paranoid psychosis after receiving ACTH for five days, which disappeared a few days after the drug was stopped. This is described in more detail elsewhere.[1] Another patient (No. 4, Table V) developed four convulsive seizures in twenty-four hours after receiving 200 mg. of cortisone daily for 11 days.[4] This did not recur when salt was restricted with subsequent courses of cortisone, despite large doses. This patient is the only one of the entire group who developed a striking "moon face." Three others listed in Table V (Cases 1, 2, and 3) developed this in mild degree. Edema was variable, but was never a serious complication, and important changes in blood pressure were not seen. Most patients gained weight, had a great increase in appetite and described themselves as feeling energetic.

COMMENT

There appears to be little doubt that cortisone and ACTH have a dramatically beneficial effect in bronchial asthma. The benefit has been almost invariably temporary and these agents can only be regarded as palliative at this time. Bronchial asthma appears to yield more readily to treatment with these agents than do most of the other diseases which are favorably influenced by them. Furthermore, relatively small doses appear to be effective as compared with that required for most other conditions. ACTH and cortisone may therefore have considerable practical value in the management of severe chronic bronchial asthma. The disadvantages of prolonged continuous treatment will undoubtedly become increasingly apparent as time goes on. One of the greatest needs at this time is the study of patients who require and are receiving continuous treatment with ACTH and cortisone.

SUMMARY

Twnty-five patients with severe bronchial asthma were treated with ACTH or cortisone by injection and cortisone by mouth in the period from December 1949 to January 1951. Treatment of bronchial asthma with these agents appears to be effective and practical. Prolonged continuous treatment of severe chronic bronchial asthma with ACTH and cortisone holds promise but will require careful study.

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ORAL CORTISONE THERAPY IN RAGWEED HAY FEVER

EMANUEL SCHWARTZ, M.D., LOUIS LEVIN, M.D., HARRY LEIBOWITZ, M.D., JACOB REICHER, M.D., JOHN F. KELLY, M.D., MILTON WALLMAN, M.D., AND THEODORE MCG. FEINBLATT, M.D., BROOKLYN, N. Y.

ORAL cortisone* and intramuscular cortisone or ACTH produce striking benefit in the symptomatic relief of bronchial asthma and associated allergic diseases.[1-9] Relief occurs within 24 to 96 hours after therapy is started and is confined to the period during, and immediately following, administration of either ACTH or cortisone. With most patients the symptoms return within several hours to two weeks after these hormones are discontinued. There is no relationship between the total dosage or duration of therapy, or both, and the length of remissions. With large doses, prolonged or repeated courses of therapy, metabolic and hormonal side effects are apt to occur more frequently.

The remarkable effects and symptomatic relief obtained cannot be ignored even though these effects may be only temporary. The symptoms of hay fever are limited, depending mostly on the duration of the pollination season. It was felt that cortisone is an ideal agent in any type of self-limited disease that would respond to its use. Also, if one were to administer the smallest possible dose to obtain therapeutic results, and exclude patients with hypertension, diabetes mellitus, hemorrhagic tendencies, peptic ulcer, congestive heart failure, coronary heart disease, pregnancy, and psychopathic personalities, the occurrence of possible side effects would be minimized.

Previous attempts have been made to treat ragweed pollinosis by the use of injectable cortisone. Carryer and associates[10] reported the use of cortisone in three cases of bronchial asthma and hay fever resulting from ragweed sensitivity. The patients were given intramuscular injections of 100 mg. daily during the ragweed hay fever season. Each patient experienced prompt relief from the symptoms of hay fever and asthma. The symptoms of asthma were more quickly relieved than those of hay fever. Relief was confined to the period during, and immediately following, cortisone administration. Friedlander and Friedlander[11] have used oral cortisone in eight patients with severe ragweed hay fever. Administration was started at a period of high pollen concentration. Coincidentally this was soon followed by a rapid fall in the pollen count and the counts remained low during the balance of the season. Remarkable symptomatic relief was experienced in six of the eight patients. It was felt that the initial symptoms were relieved by cortisone and that the continued remissions were due to the low pollen concentration present for the balance of the season.

From the Division of Allergy of the Department of Medicine, The Long Island College Hospital, and the State University College of Medicine in New York City.

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*Cortisone furnished through the courtesy of Merck & Company, Inc., Rahway, N. J.

Feinberg, Dannenberg, and Malkiel[12] treated three ragweed sensitive patients with ACTH and no relief was obtained as a result of the ACTH therapy. In their discussion they stated that, thus far, unpublished reports of the effect in hay fever have been controversial, and the impression gained is that the hormones, cortisone, and ACTH may not be very useful for that purpose. Gelfand[13] treated two patients with severe ragweed hay fever, uncontrollable by combined hyposensitization and antihistaminic therapy, with 50 mg. of cortisone on the days when the pollen count was very high, with marked clinical improvement and no adverse metabolic disturbances.

SCOPE OF STUDY

A study was undertaken to determine whether the symptoms of ragweed hay fever could be influenced by the oral use of cortisone. A total of 25 patients were included in this study. There were 4 men and 21 women, ranging in age from 21 to 60 years. The duration of hay fever varied from 2 to 18 years, and previous preseasonal and coseasonal ragweed hyposensitization ranged from 2 to 15 years' treatment. In previous years the patients experienced various degrees of relief. However, invariably the great majority of these patients had symptoms varying from slight to a marked degree during the height of the ragweed season. Although hyposensitization alone or combined with antihistamine therapy had afforded significant symptomatic relief and prevented seasonal asthma in most of the patients, the symptoms were still marked enough for them to seek further relief.

The patients were again divided roughly into three classes as to sensitiveness. This was ascertained by the strength of ragweed solution that produced a marked reaction in intracutaneous tests. The injections were given preseasonally and the largest optimal dose was attained with each patient. The top dose of ragweed extract, or a smaller one, depending upon the patient's sensitiveness, was given once weekly during the season in addition to the cortisone tablets. No other medication was administered.

It was ascertained by following the pollen counts of the previous years that the height of the season in our locality occurred approximately from August 25 to September 8. On this basis, cortisone was administered for a period of fifteen days, from August 25 to September 8 inclusive. The average pollen concentration during the period of this study was slightly higher than the average of the previous 5 years. These patients were all having hay fever symptoms at the time cortisone was started.

An attempt was made to minimize the occurrence of possible side effects. Patients with hypertension, coronary arterial disease, congestive heart failure, hemorrhagic tendencies, peptic ulcer, diabetes mellitus, pregnancy, and psychopathic personalities were not included in this study. All patients were given low sodium diets and 15 drops of a saturated solution of potassium iodide three times daily. It was felt that with these precautions and careful observation as to the side effects, it was reasonably safe to administer cortisone in the doses used for a period of 15 days.

TABLE I. RESULTS OF ORAL CORTISONE THERAPY IN RAGWEED HAY FEVER

PATIENT	SEX	PREVIOUS TREATMENT*	RESULTS†	SIDE REACTIONS	COMMENTS
1. S.G.	M	2 yrs.	4 plus	None	Excellent result. Had only slight symptoms 5 days after termination of therapy.
2. C.S.	M	4 yrs.	4 plus	None	No improvement until after the third day of cortisone therapy, then experienced excellent relief. Symptoms returned 48 hours after cessation of therapy.
3. A.C.	F	2 yrs.	4 plus	None	Complete relief of asthma which had been present for 2 yrs. Hay fever also completely relieved. Symptoms returned 48 hrs. after cessation of therapy.
4. M.R.	F	13 yrs.	4 plus	Headache and constipation	Excellent relief noted 1 hr. after start of cortisone therapy; 48 hrs. after cessation of therapy, had very severe symptoms that were relieved again within 1 hr. after resumption of cortisone.
5. E.R.	M	9 yrs.	4 plus	None	Excellent complete relief of hay fever symptoms and incidentally relief of arthritic symptoms that were present intermittently all year. Symptoms returned 48 hours after cessation of therapy.
6. A.G.	F	1 yr.	4 plus	None	Excellent relief. Still had no symptoms 3 days after cessation of treatment.
7. E.M.	F	7 yrs.	4 plus	None	Excellent result. Completely asymptomatic. Still no symptoms 5 days after termination of therapy.
8. C.P.	F	15 yrs.	3 plus	Palpitations	Obtained excellent relief of daily asthma, and good relief of hay fever symptoms. Symptoms recurred 48 hrs. after cessation of therapy.
9. T.S.	F	4 yrs.	3 plus	Insomnia	Marked relief. Only a rare occasional symptom. Still had no return of symptoms 5 days after cessation of therapy.
10. M.A.	F	2 yrs.	4 plus	Trace of sugar in urine.	Excellent results. Still feeling well 5 days after termination of treatment.
11. J.T.	F	5 yrs.	4 plus	None	Excellent result. Was still asymptomatic 5 days after cessation of treatment.
12. J.G.	M	7 yrs.	0 on 100 mg. 4 plus on 200 mg.	Collapsed during work as longshoreman. Perspired excessively. Relieved with salt tablets.	No relief of symptoms during first week on 100 mg. per day. Excellent relief on 200 mg. daily, for 3 days and then reduction to 100 mg. and relief continued. Symptoms returned within 48 hrs. after cessation of therapy.
13. M.W.	F	15 yrs.	4 plus	Trace of sugar in urine.	Excellent result. Asymptomatic 3 days after termination of therapy.
14. M.M.	F	1 yr.	0	None	Patient very uncooperative. Did not follow instructions. Did not take the cortisone regularly. Claims she felt better last year.

TABLE I—CONT'D

PATIENT	SEX	PREVIOUS TREATMENT*	RESULTS†	SIDE REACTIONS	COMMENTS
15. M.D.	F	3 yrs.	4 plus	None	Excellent result. Completely asymptomatic. Symptoms returned 48 hrs. after cessation of therapy.
16. D.R.	F	1 yr.	2 plus	None	No relief until the 4th day of treatment. Then experienced moderate improvement. Felt better the previous year. Symptoms returned within 24 hours after cessation of treatment.
17. H.Y.	F	1 yr.	4 plus	None	Obtained complete relief of both her asthma and hay fever after the 2nd tablet. Excellent result. The symptoms recurred within 48 hours after cessation of therapy.
18. J.M.	F	1 yr.	3 plus	None	Asymptomatic for first 10 days of treatment. Then had some moderate symptoms with a purulent nasal discharge which patient thought was due to an upper respiratory infection.
19. R.R.	F	3 yrs.	3 plus	1 day of abdominal pain, belching, nausea, diarrhea at onset.	Marked relief after first day. Occasional slight symptom. Return of symptoms 48 hours after cessation of treatment.
20. A.D.	F	6 yrs.	4 plus	Headache and precordial pain	Excellent result. Could sleep through the night for the first time during any hay fever season.
21. M.S.	F	13 yrs.	4 plus	Palpitations	Excellent relief. This was first time her asthma was relieved during hay fever season. No other symptom. Still no return of symptoms 3 days after cessation of therapy.
22. L.D.	F	4 yrs.	3 plus	None	Marked relief. Had an occasional symptom. Felt much better than last year. Symptoms returned 3 days after termination of therapy.
23. M.B.	F	4 yrs.	3 plus	Insomnia	Marked relief. Experienced best year in 15 years of hay fever. Had only an occasional symptom. Had gradual return of symptoms 2 days after termination of therapy.
24. G.R.	F	12 yrs.	4 plus	Headache, weakness, nervousness on 2nd day of therapy only.	Excellent relief of hay fever symptoms starting on 2nd day of therapy. Had previously had a closed tear duct which caused great discomfort during hay fever season because of continuous flow of tears from eyes. This was greatly relieved. Only had a slight moisture from eye. Symptoms returned 48 hours after termination of therapy.
25. R.K.	F	3 yrs.	0	Discontinued therapy.	After 6th tablet developed dizziness, nausea, and vomiting and was unable to continue medication. No relief of symptoms.

All patients received cortisone for 15 days unless otherwise noted. Daily dose, 100 mg.

*Ragweed hyposensitization.

†4 plus – excellent relief of symptoms.
3 plus – marked relief of symptoms.
2 plus – moderate relief of symptoms.
0 – no relief.

DOSAGE SCHEDULE

The dosage schedule consisted of 25 mg. of cortisone 4 times a day, a total daily dose of 100 mg. Twenty-four patients were able to tolerate this dose very well. One patient complained of dizziness, nausea, and vomiting and discontinued cortisone after the sixth dose.

RESULTS OF TREATMENT

Oral cortisone in doses of 25 mg. 4 times a day remarkably relieved the usual symptoms of ragweed hay fever in 21 of 25 patients selected for this study. Fifteen patients obtained excellent relief, and 6 patients, marked relief. One patient experienced moderate relief, and 3 patients, no relief (Table I). Case 12 was classified as a failure since on the dosage used in this study (100 mg. daily) he had no relief of symptoms. However, he experienced excellent relief when the dose was increased to 200 mg. daily, without side effects. In those patients who obtained relief it was far superior to that produced by any other previous treatment. Relief occurred in from one to 72 hours after the beginning of therapy. In general, the maximum relief of symptoms was obtained by the third day of treatment. The patients continued asymptomatic as long as oral cortisone was administered. Discontinuation of cortisone resulted in a recurrence of symptoms. In 15 patients there was a return of symptoms in 48 hours.

In one patient, treatment was discontinued because of dizziness, nausea, and vomiting after the sixth tablet. A transient, slight glycosuria occurred in two cases. Other side effects consisted of headache in 3 cases, palpitations in 2, insomnia in 2, precordial pain in 1, constipation in 1, abdominal cramps, nausea and diarrhea in 1 case, and weakness and nervousness in 1 case. These side effects were mild and of brief duration. They did not interfere with the continuation of cortisone. The majority of patients stated that they were able to be more active and many were engaged in increased physical activity while taking cortisone. It was noted that most patients experienced an initial weight loss of 2 to 3 pounds. This may have been due to the low salt diet. There were no significant changes in blood pressure in any of the cases.

DISCUSSION

Cortisone therapy is not a substitute for hyposensitization. Only by the production of blocking antibodies can one ultimately obtain complete and lasting benefit. It is also by this method that the patients are less prone to develop asthma.

However, the good results obtained with cortisone in this series of cases far surpassed any previously obtained by hyposensitization and/or antihistamine therapy. Cortisone should be reserved, however, for those cases in which the indications are strong, i.e., in those patients who have marked symptoms during the height of the season, after the usual therapeutic measures, such as hyposensitization and antihistamines have failed. No serious side effects occurred in this series. In order the minimize the occurrence of side effects one should

be careful not to administer cortisone to hay fever patients who have a coexisting hypertension, coronary arterial disease, congestive heart failure, hemorrhagic tendencies, peptic ulcer, diabetes mellitus, pregnancy, or psychopathic personalities. It was found that short term therapy could be carried out safely without extensive laboratory tests if there were proper cooperation between patient and physician and careful observation as to the possible occurrence of side effects. The patient's weight, fluid intake and output, blood pressure, and the results of the urine examination for sugar should be charted daily. To further minimize the possible occurrence of side effects the patients were given a low sodium diet and potassium iodide. The relatively small dose of 100 mg. of cortisone daily and the short duration of therapy (15 days) were other factors that also possibly minimized the occurrence of severe side effects. The dosage schedule was arbitrarily adjusted to 25 mg. of cortisone four times daily, a total of 100 mg. per day. It is possible that a smaller dose of cortisone, either alone or in combination with an antihistamine, may produce the same symptomatic relief and further decrease the incidence or severity of possible side effects.

SUMMARY

1. Twenty-five selected hay fever patients were treated with oral cortisone tablets in addition to preseasonal and coseasonal ragweed hyposensitization. There were 21 women and 4 men, ranging in age from 21 to 60 years. The duration of their hay fever was from 2 to 18 years, and the duration of previous ragweed hyposensitization ranged from 1 to 15 years.

2. Twenty-one of the 25 patients obtained marked or complete relief. Fifteen obtained excellent or complete relief; 6, marked relief; 1, moderate relief, and 3 patients had no relief of symptoms.

3. Side effects were observed in 10 patients, and in 9 they were mild and of brief duration and did not interfere with the continuation of cortisone. One patient discontinued its use because of dizziness, nausea, and vomiting. No severe side effects were encountered in this series.

4. Oral cortisone therapy combined with hyposensitization in ragweed hay fever produced much greater relief than that obtained previously with any other treatment. The results justify its use in selected cases after the usual therapeutic measures have failed.

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ROENTGEN STUDIES OF ALLERGIC CHILDREN WITH DISTURBANCES OF THE PYLORUS RESULTING FROM FOOD SENSITIVITY

JOSEPH H. FRIES, M.D.*
BROOKLYN, N. Y.

VISUALIZATION of allergic manifestations of the gastrointestinal tract has been made possible by the roentgenogram. Two previous communications of the author's on this subject have dealth with the method used and the alterations obtained.[1, 2]

It is becoming increasingly apparent that the pylorus plays a major role in the allergic symptomatology of the stomach, and that any survey of the many factors underlying pyloric obstruction must include hypersensitiveness.

HISTORICAL

Roentgenographically observed changes in the gastrointestinal tract, including spasm of the pyloric antrum produced by an antigenic food, were first reported by Holtzknecht in 1906.[3] Subsequently, spasm and obstruction of the pylorus with gastric retention were found on the roentgenograms of food-sensitive patients by several authors.[4-8] At laparotomy, the abnormality, in some instances, was found to be due to angioneurotic edema.[9-12] Several authors have observed edema of the pylorus on gastroscopy, following administration of allergenic substances.[13-17] Walzer passively sensitized areas of gastric mucous membrane in the rhesus monkey. Exposure to the antigen produced allergic reactions consisting of edema and of spasm of the stomach, including the pyloric region.[18, 19]

Intentional feeding of a known allergenic substance for the purpose of inducing roentgenographic changes, and the use of a contrast meal of plain barium was reported first by Serio,[20] and later by Rowe.[21] These were followed by the writer's earlier studies on children,[1, 2] which have since been corroborated by other workers.[22, 23]

PROCEDURE

Thirty allergic children, ranging in age from 4 to 14 years, were selected for this investigation. All had repeatedly exhibited marked gastrointestinal disturbances (vomiting, abdominal cramping, nausea, and epigastric distress) within a few minutes after ingestion of small amounts of offending foods. Many of these children showed positive intracutaneous reactions to tests with the offending food.

In the control roentgenographic study, plain barium sulfate and water were used.

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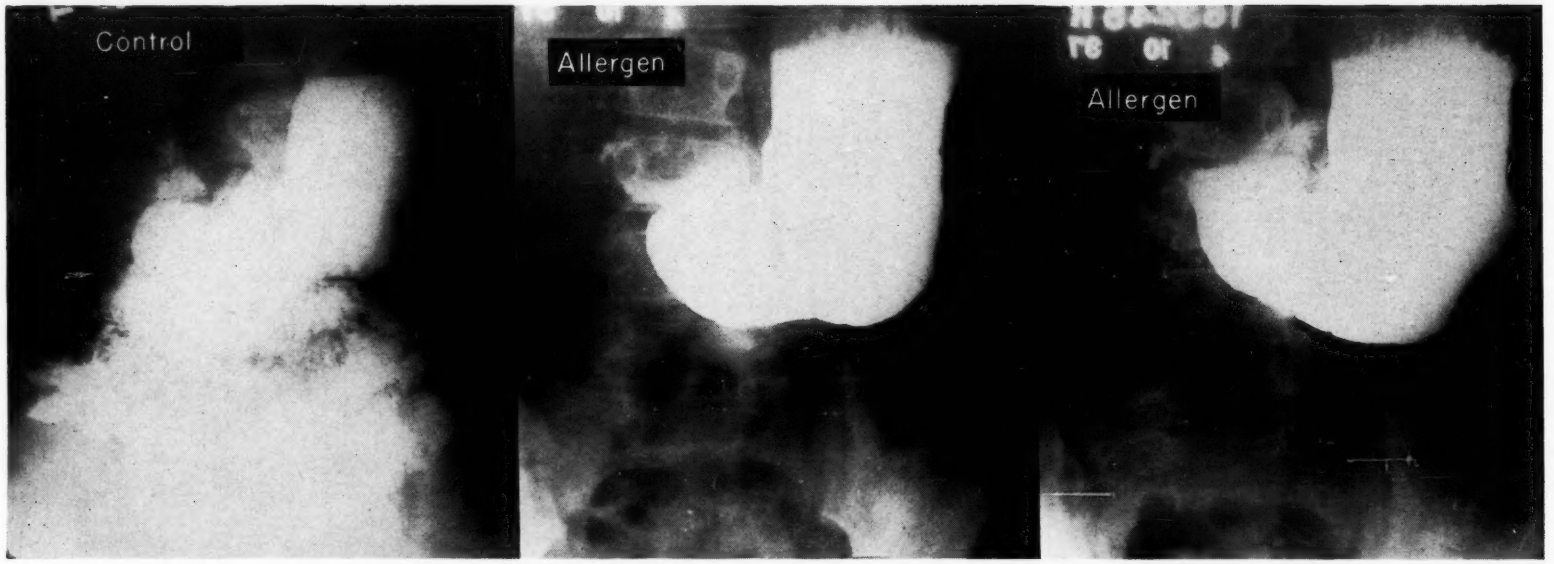
*From the Division of Allergy, Jewish Hospital of Brooklyn.



A. *B.* *C.*

Fig. 1.—(Case LKN) Patterns characteristic of those observed during fluoroscopy. *A*, Control study made 20 minutes after ingestion of plain barium meal showing normal pylorus and free passage of barium. *B*, Study made 20 minutes after ingestion of allergen-barium containing 4 ml. of egg, showing abnormal pylorus and delayed emptying of stomach. *C*, At 40 minutes findings persist.

Approximately a week later, a similar study was made, employing barium sulfate and water, to which the offending allergen was added without the knowledge of the patient. Previous trials had revealed the amount of allergens that would be needed to produce a pronounced gastrointestinal disturbance. These varied from 2 c.c. to 12 c.c. (½ to 3 drams). Such amounts, in normal subjects, proved insufficient to alter the normal roentgenogram.[2]

During the first 30 minutes of both series, most of the patients were subjected to intermittent fluoroscopy. Roentgenograms were then taken at ½ hour, 1, 2, 3, and 6 hour intervals.

Fluoroscopic Findings.—In the control series, the barium began to leave the stomach immediately, or within ten minutes after ingestion, which, according to Hefke,[24] is the normal "pyloric opening time." (Table I.)

TABLE I. PYLORIC OPENING TIME AFTER ALLERGEN-BARIUM MEAL
28 SUBJECTS

TIME	NUMBER OF SUBJECTS	PERCENTAGE
Over 20 minutes	9	32
20 minutes	8	28
15 minutes	3	11
10 minutes	5	18
5 minutes	3	11
Prolonged emptying time (15 or more minutes)	20	82
Normal emptying time (less than 15 minutes)	8	18

In the allergen series, a delay of 20 minutes or longer in the passage of allergen-barium from the stomach to the duodenum was observed in 20 of the 28 children who were studied by fluoroscopy.

In some instances, a persistent or intermittent narrowing of the pyloric canal was noted. With the opening of the pyloric sphincter, the allergen-containing barium issued irregularly into the small intestine in the form of separate boluses. In view of this scant release of barium, the duodenum was difficult to visualize. When discernible, it appeared narrow or distorted, and in some instances the rugal folds were clearly visible.

These changes in the pylorus were accompanied by abdominal pain with a persistent point of tenderness in the epigastric region, epigastric distress, and in some instances by vomiting.

Coincident with these findings, gastric peristalsis was diminished or absent in 17 subjects. Hypotonicity of the stomach was observed in 14 of these.

Roentgenographic Findings.—The roentgenograms in most part confirmed the fluoroscopic findings.

The first film, taken at 30 minutes, generally revealed poor passage of allergen-barium into the small intestine. Only a few small globules were visualized in the duodenum and jejunum. In later films, globs of barium of varying size were strung out irregularly throughout the small intestine.

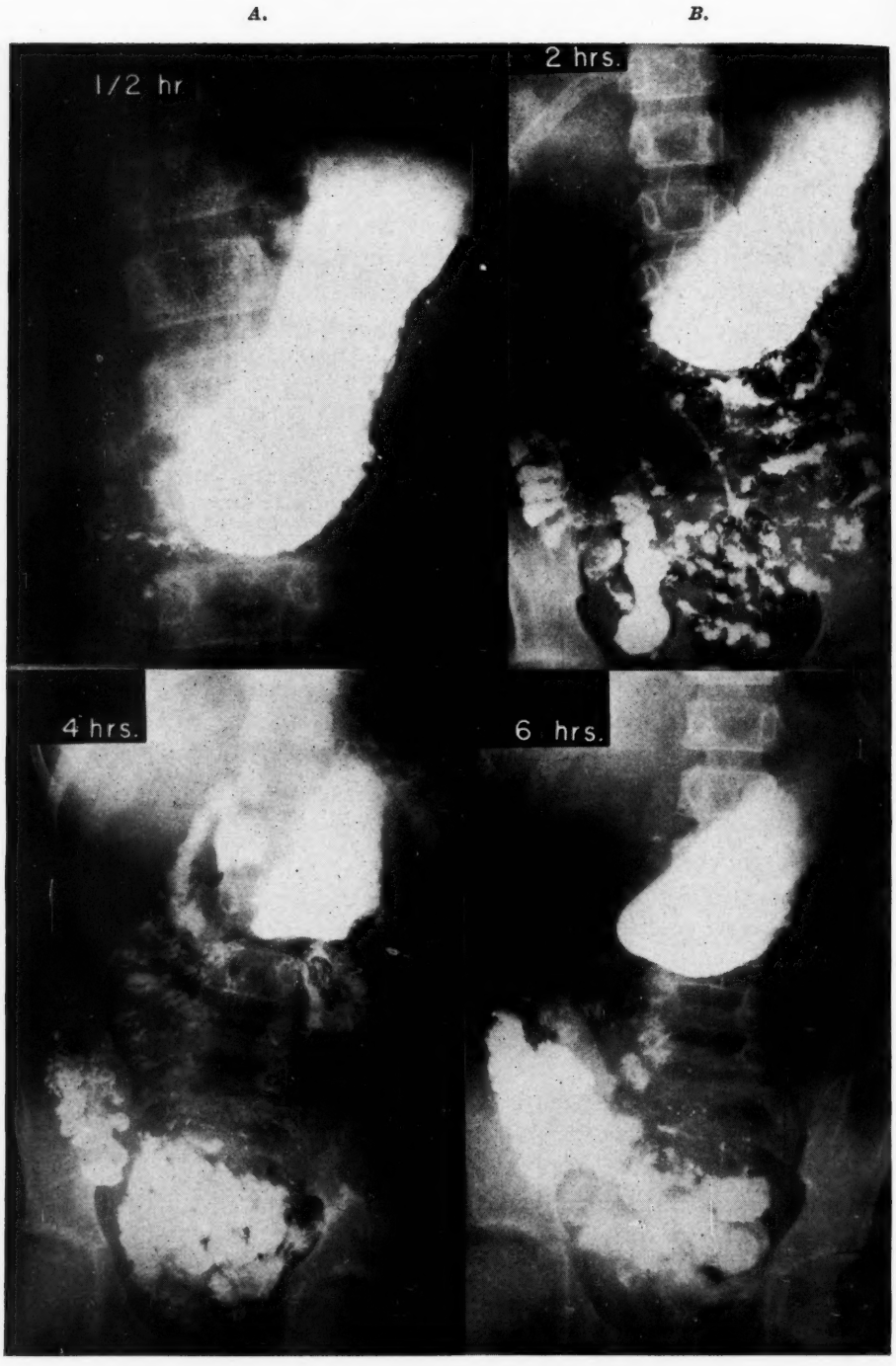


Fig. 2.—(Case LUB) Serial roentgenograms following ingestion of allergen-barium (egg). *A*, At ½ hour, pylorus is indistinct and stomach does not empty. *B*, At 2 hours, pylorus is indistinct and there is marked segmentation of barium in small intestine. *C*, At 4 hours, pylorus is still obscured. *D*, At 6 hours, pylorus is not visualized and gastric retention is obvious.

The most striking alterations in the allergen-barium series were found in the pylorus. In many instances the antrum and/or pyloric canal were obscured for as long as six hours. Occasionally, the outlines of the pylorus were irregular, changing slightly from hour to hour. These irregularities resembled those commonly obtained with reflex pylorospasm, or with eroding, infiltrating or stenotic lesions caused by malignancy, or ulcer. The duration of the pyloric alterations varied. (Table II.)

TABLE II. AMOUNT OF GASTRIC RETENTION 6 HOURS AFTER ALLERGEN-BARIUM MEAL
13 SUBJECTS—15 TRIALS

PER CENT OF GASTRIC RETENTION	NO. OF TRIALS	ALLERGEN USED
66	1	Nut
50	2	Nut, Corn
33	3	Egg (2), Nut
25	3	Egg (2), Milk
20	2	Egg, Cabbage
15	4	Egg, Chocolate (2), Wheat

In 13 subjects, gastric retention ranging from 10 per cent to 66 per cent was observed at the 6-hour period, at which time the pylorus often still showed a deformity. The controls showed no gastric retention (Table II).

With 3 patients, studies with the same allergen were repeated on different days. Similar involvement of the pylorus occurred each time.

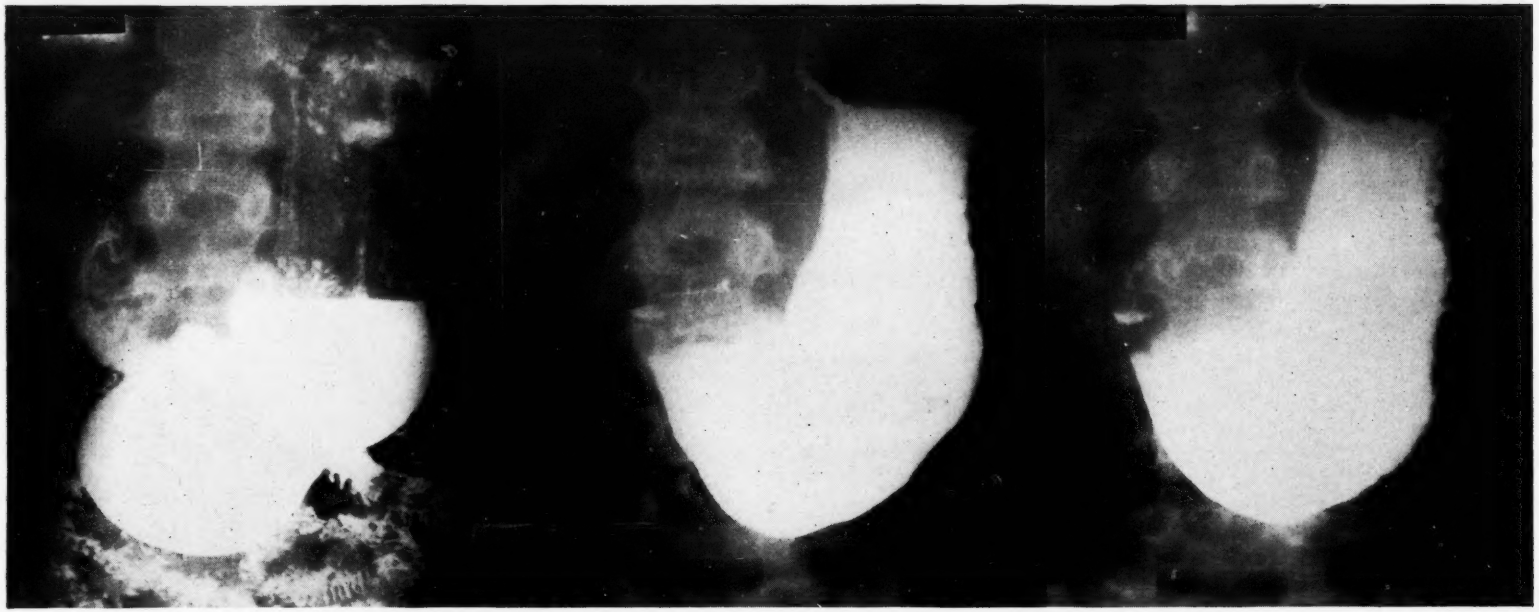
One patient, sensitive to three different foods (egg, fish, and nut), responded on different occasions with the same gastrointestinal symptoms after trial feeding with each of these offenders. Involvement of the pylorus was demonstrated by roentgenogram in each instance.

DISCUSSION

The present study seems to support the findings of earlier workers who, by gastroscopic examination of the stomach during an allergic reaction, observed that the involvement seemed primarily to involve the pyloric region.[16, 17] It is the author's impression based on his own studies that an allergic reaction in the region of the pylorus might account for the epigastric distress, the cramplike nature of the pains, and the rapid onset of symptoms following ingestion. The spontaneous relief which follows elimination of the antigen either by vomiting or passage to the lower bowel suggests a contact reaction. This is further substantiated by the author's previous studies involving rectal instillation of the antigen where contact provoked immediate onset of symptoms which were accompanied by spasm observable roentgenographically in the large intestine.

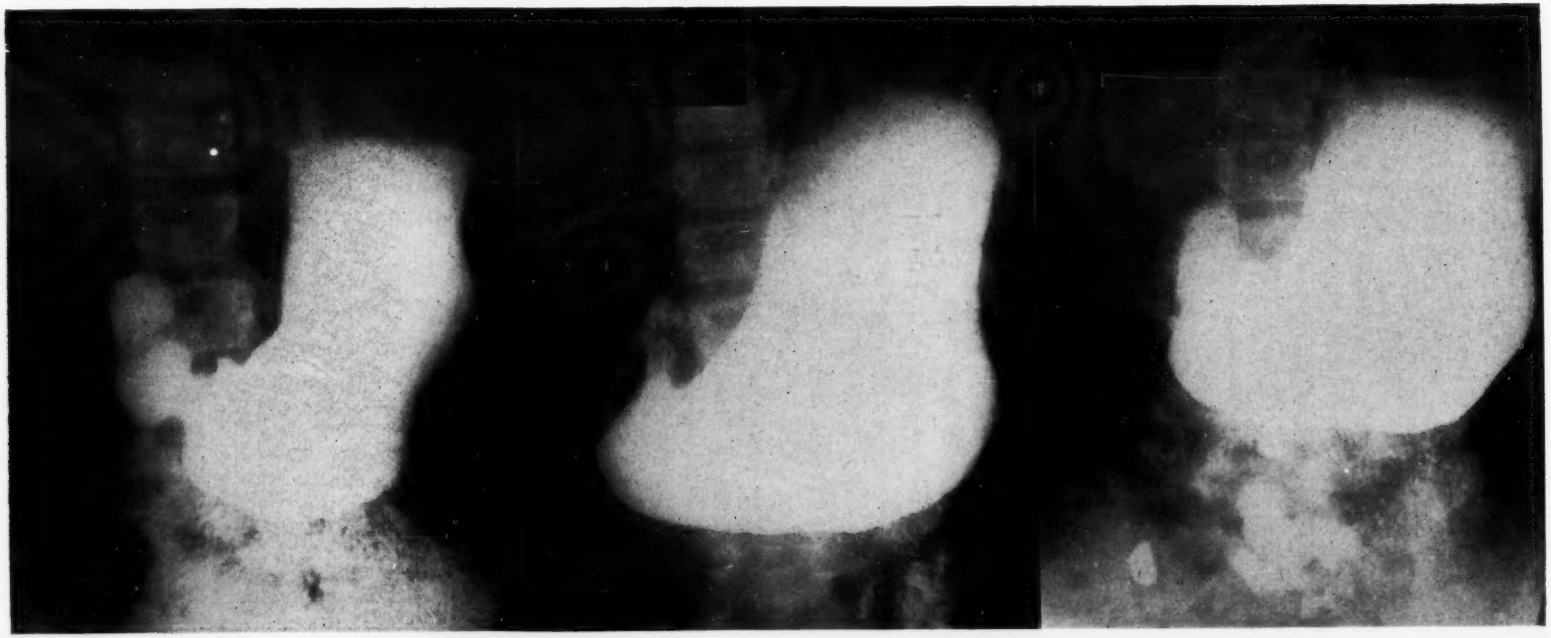
Embryologically, the pylorus is a separate organ. Even in a 10 mm. embryo, the stomach is already developed into an expanded pars-cardiaca and a tubular pars-pylorica.[25] Therefore, it is logical to find the pylorus acting independent of, and at variance with, the stomach.

The physiology of the pylorus may explain the magnitude of its allergic reactivity. It is a thick, highly contractile, muscular organ, with a narrowed lumen and large mucosal folds. In response to an offending allergen, these



A. *B.* *C.*

Fig. 3.—(Case LTZ) *A*, Control study 30 minutes after ingestion of barium meal showing normal outlines. *B*, Comparative study 30 minutes after ingestion of barium containing 6 ml. of egg, showing distorted pylorus and persistent small deposit of barium in base of duodenal cap, simulating pocket formation of ulcer. *C*, At one hour, abnormality still persists; hypotonicity and delayed emptying of stomach is observable.



A. *B.* *C.*

Fig. 4.—(Case VOC) *A*, Control study, 30 minutes after barium meal, without allergen. Pylorus and gastric emptying are normal. *B*, Allergen study 30 minutes after ingestion of barium and 30 ml. of milk. There is stenosis of juxta-pyloric region resembling malignancy. *C*, At 60 minutes after allergen-barium meal there are sparse, irregular masses of barium in the intestine. The alterations in the pylorus persist.

mucosal folds enlarge, and in some instances, accompanied by a spasm of the pylorus, produce the narrowing or obliteration of the lumen which is demonstrable on roentgenogram.

Not all of the gastric retention observed can be attributed to the pyloric obstruction alone. In many instances, the stomach also participated in the reaction—with decreased tone and diminished peristalsis, instead of the increased peristalsis which frequently accompanies pyloric obstruction.

Several of the roentgenograms of the allergen series gave fairly good outlines of the mucosal pattern of the stomach, some of which revealed increased prominence of the gastric folds. This is in accordance with previously reported findings.[6, 8, 16]

Lesions induced by an allergic reaction may resemble those of organic disease. However, the changes resulting from organic lesions are constant. When the alteration is caused by transient angio-edema of allergic origin, with or without spasm, as described in this study, the configuration changes on repeated inspection of the same region.

CONCLUSIONS

1. Allergic reactions occurring in the stomach following intentional feeding of antigenic substances are often most pronounced in the pyloric area.

2. These reactions are often discernible and reproducible. They disappear with the termination of the allergic reaction.

3. The gastric retention reported in this and in previous studies of the author's may be attributable mainly to blockage of the pylorus.

4. The roentgenograms reveal transient abnormalities whose configurations sometimes resemble those of fixed organic lesions.

5. Re-exposure to the same allergens resulted in reactivation of the same shock tissues. Exposure to other antigenic foods producing the same symptoms in the same patient also produced similar allergic responses in the pylorus.

6. In the interpretation of abnormalities of the pylorus, as revealed on roentgenogram, the possibility of allergic involvement must be considered.

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A PRELIMINARY POLLEN ANALYSIS OF THE MIAMI, FLORIDA, AREA

LILLIAN BEAMAN FLY,* COCONUT GROVE, FLA.

IT IS the purpose of this paper to present some aerobiological data concerning the Miami, Florida, area and contiguous regions. The data presented were gathered over a two-year period extending from March 31, 1947 to March 31, 1949. This report should not be considered in any way complete for an area with such a diverse native and exotic flora. However, an attempt has been made to be selective of the material presented in order to make available representative information which may be useful in academic and applied botany as well as medical studies.

When the problem of conducting an aerobiological survey, with particular reference to pollens, was undertaken it became apparent that the reference data upon which such a study is based were almost completely lacking for this geographic area. These data consist of a botanical field survey to determine pollinating periods, the organization of a reference collection of known pollens for identification purposes, the tabulation of meteorological data, and finally the correlation of air-load factors with this information.

Until the aegis of studies of pollens as etiologic agents in certain pathologic reactions, the science of aerobiology in relation to pollens did not exist. Ray,[58] in 1693, made one of the earliest observations of the role of wind in the dissemination of pollen. He stated in his *Historia Plantarum:*

"When artificial pollination (of the date palm) cannot take place, the wind may possibly answer the same purpose."

Apparently this phase of pollen study attracted little attention until the thorough investigations of Sprengel,[58] who conducted a complete study of flower pollination in 1812. It is of historic interest in aerobiology that he noted definite distinctions between anemophilous and entomophilous plants. He correlated the type of flower parts, lack of nectar, lightness and shape of pollen grains with their air-borne habit. Many observations of the presence of pollen grains in the atmosphere were made from time to time, but no systematic study of their incidence was undertaken until there was some need for quantitative data. The study of "pollen disease," which developed into the branch of medicine known as allergy, presented this need.

This study required the cooperation of many individuals. I am particularly grateful to: Dr. Taylor R. Alexander, Chairman; Professor Roy Woodbury; Dr. R. Bruce Ledin; Dr. Walter Buswell; all of the University of Miami Botany Department. I greatly appreciated the courtesy of the Jackson Memorial Hospital Library staff, and helpful suggestions made by Dr. Nelson Zivitz.

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*Botany Department, University of Miami, Coral Gables, Florida.

Durham,[15] referring to Blackley who began a study of the pollen content of the air in Manchester, England, in 1866, wrote, "the first serious investigation of pollen incidence was as premature as it was excellent." Blackley's work was done long before there was general acceptance of the pollen theory of hay fever, yet his first series of observations, completed in 1873, established pollens as the cause of certain respiratory disorders.

Interest in further studies lagged, however, until some practical clinical method was devised to counteract "pollen disease." Ragweed and grass sensitizations were the first types of pollinosis to receive extensive study. These investigations stimulated interest in other plants as possible allergens. It was logical that the studies began with the strictly air-borne pollens.

Scheppegrell[45] began exposing slides to obtain daily pollen counts in New Orleans in 1916, and presented in 1921 one of the first comprehensive quantitative reports. It was not until 1925, however, that similar studies were undertaken in other parts of the United States. When the value of pollen counts became evident there was a deluge of reports on local surveys. These surveys were helpful but were so filled with "unknowns" because of the lack of field studies that most of the botanists working in allergy placed slide counting secondary to correlated field observations. Cooke[9] referred to the work of Hodgson, botanist of the Department of Allergy at Roosevelt Hospital, New York:

"Hodgson, whose experience in pollen surveys and pollen counting extends over a period of thirty years, maintains that daily field surveys give a more accurate idea of the different pollens encountered in a given area, and that pollen counting should be used merely as a supplement to this."

As the studies of aerobiology in relation to pollen incidence advanced it became increasingly evident that pollen analysis in any geographic area involved investigations of: first, determination of pollen chronology; second, the establishment of an identification collection; and third, the compilation of the various climatic factors connected with dispersion. This is particularly true in southern Florida. This area, though part of continental United States, is ecologically the northernmost extension of the West Indies.[11] Therefore, this region constitutes an area unique in the United States. One pollen survey that has been published for the Miami area[37] was difficult to evaluate due to lack of correlation with field studies or meteorologic data. Consequently, it became obvious at the outset of this investigation that the organization of reference data was necessary in order to derive any significant information useful in any of the fields of botany or medicine concerned.

The first step was compilation of information on the pollinating periods of representative flora. This was done by making frequent field observations and illustrating these data graphically following the method of Hodgson (Fig. 1). Inasmuch as the method of pollination of many of the plants in this area has not been determined, no designation of this factor was made on the figure. In establishing the chronology of pollens, the periods demonstrated represent the duration of the flowering time of the plants involved. Slide counts of pollens were not considered in this case.

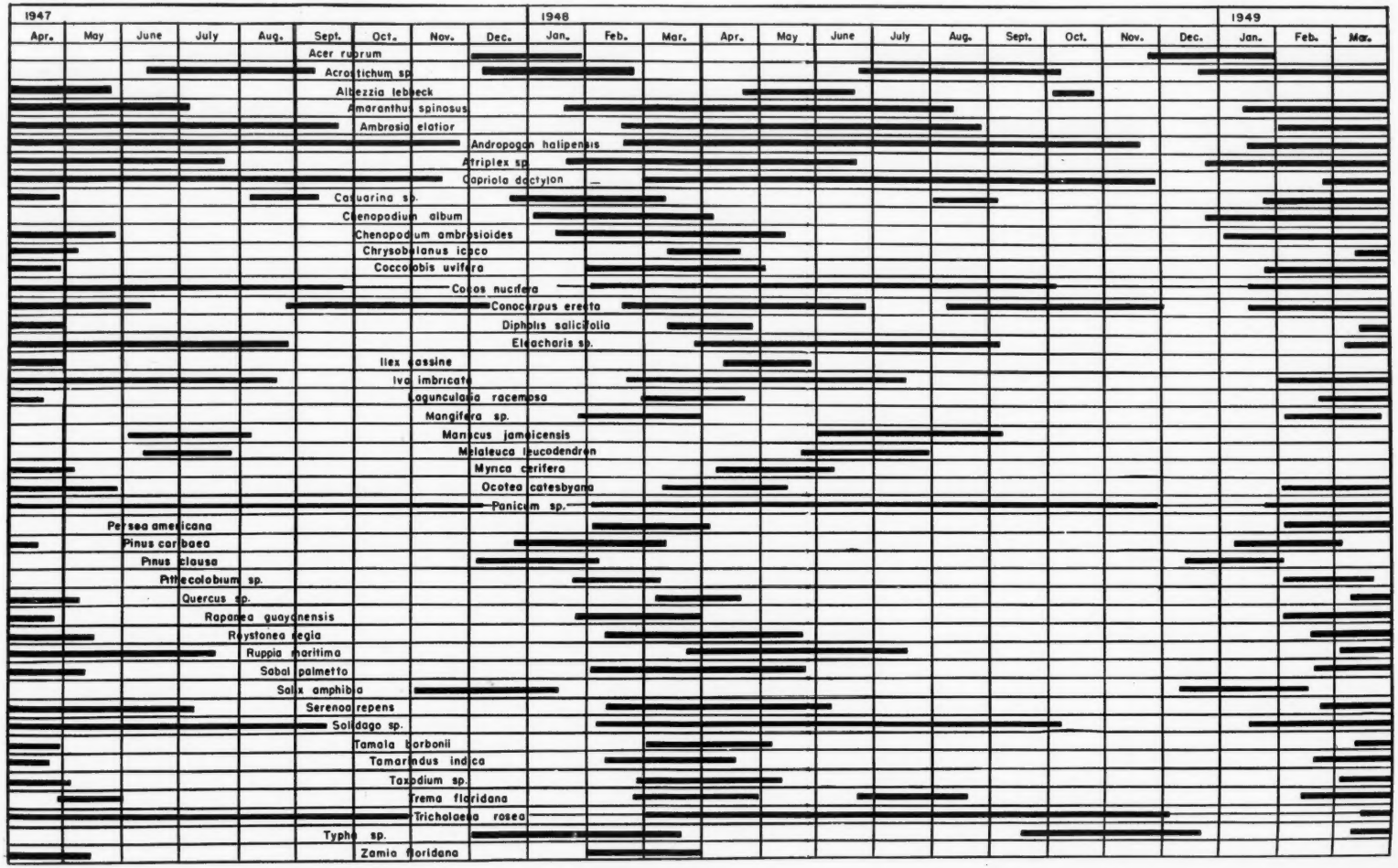


Fig. 1.—Chronology of pollens in the Miami area. For list of common names used see page 55.

The second step was carried out concurrently with the field studies to determine the chronology of pollinating periods. This consisted of collecting pollens and preparing them for reference. The known pollens were defatted and dehydrated with xylol then mounted in balsam. In this type of preparation the grains appear unstained and unexpanded as they do when collected in the field or on air exposure slides.

The third of these basic reference materials was the preparation of detailed summaries of meteorologic data. These data were obtained from readings made from standard constant recording instruments placed on the campuses of the University of Miami. Wind direction and wind velocity figures were obtained from the official summaries of the United States Weather Bureau station in Miami. The computations are 24-hour averages based on 2-hour interval graphs according to preferred statistical methods.[38]

During the two years of this investigation a determination of the pollen air-load was made. The method used was the standard technique approved by the National Pollen Survey Committee of the American Academy of Allergy in 1946.[39] This method standardized pollen count reports as the number of grains per square centimeter of slide area. The counts were made from slides exposed under the conditions specified and on an apparatus approved by the committee. This method was followed whenever feasible. However, it was apparent at the outset of this study that the standard procedures of aerobiologic analysis had to be modified to meet the exigencies imposed by the physiographic and meteorologic conditions of this region. Constant high humidity made it necessary to use petroleum jelly on exposure slides rather than glycerin jelly. In order to insure more accurate counts of a low air-load three slides were exposed at a time.[60] The modifications were so made that the results could be compared with those obtained throughout the United States. It was found that only from the middle of March to the first week in May was the total pollen air-load heavy enough to make this type of count significant. Consequently, correlative data were of necessity confined to a time period in which all the factors could be demonstrated.

Since only during a two month period of each year was there a discernible pollen incidence, several tentative explanations have been made to account for the lack of air-borne pollens in an area which might be expected to maintain a relatively heavy air-load. It was thought that the almost constant moderate southeast winds directly from the Atlantic Ocean would "clear" the air of pollens by blowing air-borne particles inland. Another possibility investigated was that the consistently high relative humidity would tend to keep normally buoyant pollens close to their source.

In order to examine these possibilities a chart was prepared to illustrate graphically the meteorologic factors involved (Fig. 2). The month of April, 1947, was chosen in order to correlate a total pollen air-load with these factors. During this time period, *Pinus caribaea* (Caribbean pine) was pollinating and thus afforded the opportunity to obtain a high enough count by standard methods to be significant. Notations on the chart indicate daily averages for the factors involved with the exception of rainfall for which weekly totals are designated.

Fig. 1.—Chronology of pollens in the Miami area. For list of common names used see page 55.

The data obtained seem to indicate that wind velocity and direction had very little bearing on the maintenance of an air-load of a known anemophilous pollen. The rather small variations in relative humidity, which did not go below seventy-three per cent for the four week period, apparently did not affect the buoyancy of the pollen. The only factor which was demonstrated to have any bearing on diminishing the air-load was direct precipitation of rain. The possibility of low pollen production for this selected time period is not acceptable since the total pollen count compares favorably with the figures obtained in 1948 and 1949 in this investigation and with the data presented by Nichol and Durham in 1931.[37]

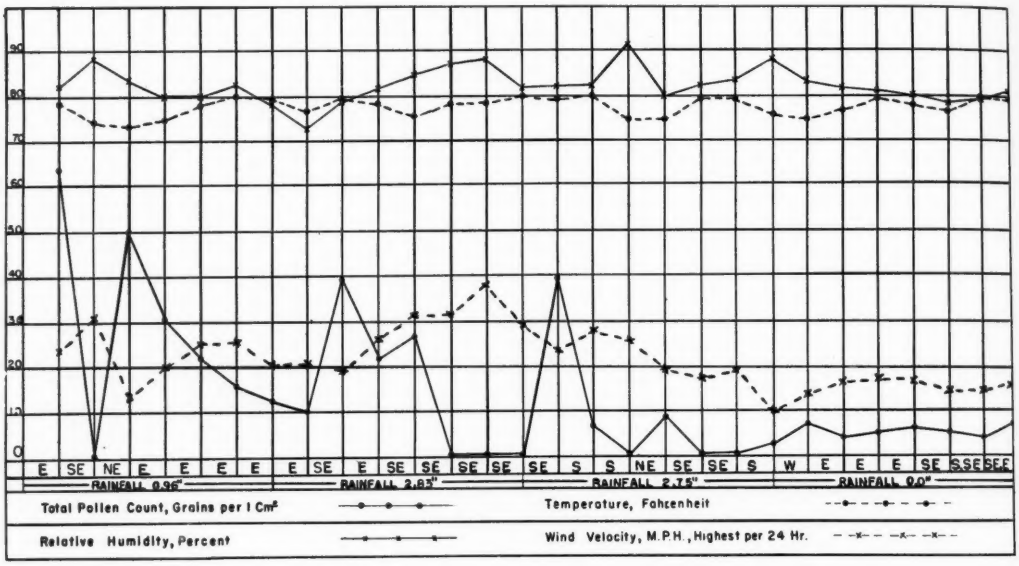

E SE NE E E E E E SE E SE SE SE SE SE S S NE SE SE S W E E E SE SSE SE
RAINFALL 0.96"
RAINFALL 2.83"
RAINFALL 2.75"
RAINFALL 0.0"
Total Pollen Count, Grains per 1 Cm²
Temperature, Fahrenheit
Relative Humidity, Percent
Wind Velocity, M.P.H., Highest per 24 Hr.

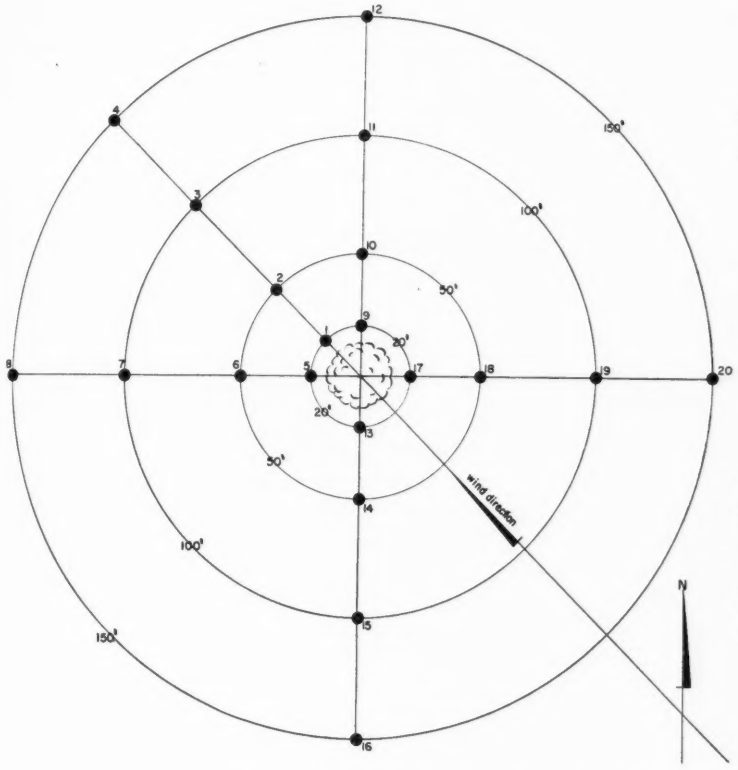
Fig. 2.—Correlation of total pollen airload with either data (April, 1947).

With the exception of precipitation it was not demonstrated that meteorologic factors affected the presence in the air of a pollen which is anemophilous in all its geographic range. Therefore it was reasonable to assume that these factors would not influence the incidence or, more accurately, the absence of other pollens whose dispersion behavior may be modified by this environment.

Since in the literature available there was found no precedent for determining the radial dispersion of pollens a method was devised to check the dispersion of pollens at the source. In an attempt to determine the distance pollen was carried from the plant or plants a radial transect was laid out. Isolated plants in flower were selected. Using the center of the stand or the bole of a tree as a hub, the radii were determined with a compass and extended with a metal tape. On each radius exposure stands were placed at the desired intervals. Radial transects are illustrated graphically in Figs. 3 and 4. This method is given simply as a possible approach to some of the problems involved in an ecologic investigation in subtropic Florida.

In order for the results of dispersion studies to have any validity, species were selected which had exhibited deviations in pollinating habits which could not be explained by their reaction to the atmospheric environment into which their pollens were shed. Consequently, ragweed and "woman's tongue" were selected to demonstrate contrasting pollinating deviations.

Ragweed has been the classic wind-pollinated plant of medical and economic significance. *Ambrosia elatior*, the short ragweed of allergy literature, grows to a height of 6 feet or more in south Florida. Why this particular species should display such phenomenal vegetative growth might be answered by studies in anatomy,[57] physiology, cytology, ecology,[25] and photoperiodism or temperature, singly or interrelated.[26] However, the most striking observations in the modified behavior pattern are the dispersion of pollen and the length of the pollinating period.



STATION NUMBER	NO. GRAINS ON SLIDE
1	22
2	5
3	5
4	0
5	18
6	3
7	0
8	0
9	19
10	1
11	0
12	0
13	17
14	0
15	0
16	0
17	18
18	1
19	0
20	0

Slide stations read quantitatively after 12-hour exposure.

Transect set at 7 A.M.

Slide stations approximately 5 feet above ground.

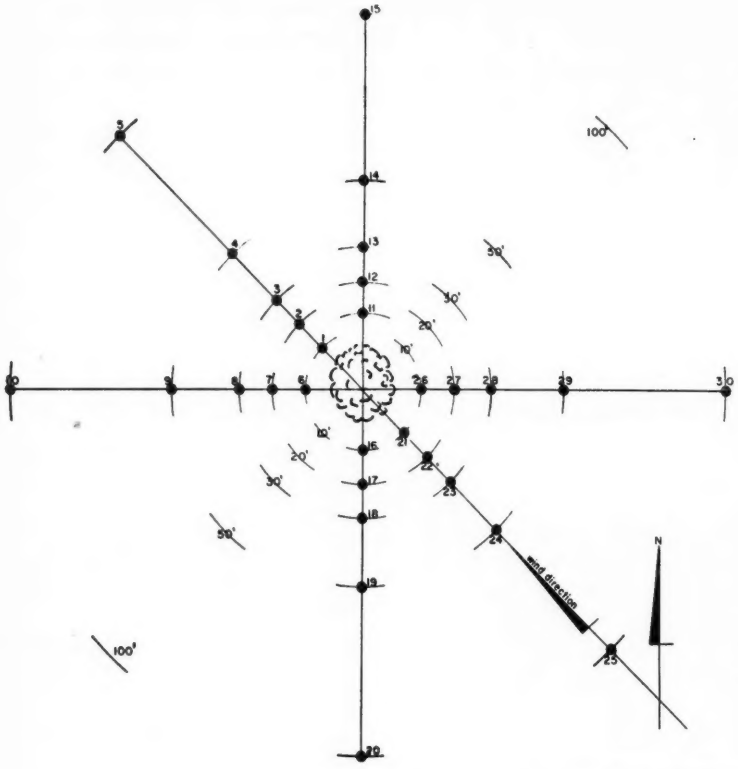
Wind direction southeast, moderate.

Slide station indicated.

Fig. 3.—Radial dispersion of *Albizza lebbek* pollen.

During the entire seven month pollinating period of *Ambrosia elatior* (Fig. 1) in 1947, only 20 grains were counted on exposure slides. Nichol and Durham[37] in 1929 found 61 grains. Correlated with this are reports of very few proved clinical cases of ragweed pollinosis in this area.[62] Field observations on anthers indicated that mature pollen was produced in quantities comparable to that produced in areas where ragweed has a significant air-load density. Yet

pollen was not found on exposure slides in a ratio comparable to the expected density. A radial transect was arranged around an isolated stand of ragweed as illustrated in Fig. 4. The slide counts given are averages of five separate readings. The conclusion, from even such a cursory study, would seem to be that *Ambrosia elatior,* in the environment imposed by this region, could not be regarded as a strictly anemophilous plant. Medical evidence bears out this conclusion.[62] The reasons for this behavior have not been determined but the dispersion problem has been approached.



STATION NUMBER	NUMBER OF GRAINS		
	10 A.M.	1 P.M.	4 P.M.
1	5	2	0
2	3	1	0
3	2	0	0
4	0	0	0
5	0	0	0
6	2	0	0
7	0	0	0
8	0	0	0
9	0	0	0
10	0	0	0
11	1	0	0
12	1	0	0
13	0	0	0
14	0	0	0
15	0	0	0
16	1	0	0
17	0	0	0
18	0	0	0
19	0	0	0
20	0	0	0
21	0	0	0
22	0	0	0
23	0	0	0
24	0	0	0
25	0	0	0
26	1	0	0
27	0	0	0
28	0	0	0
29	0	0	0
30	0	0	0

Wind direction southeast, moderate
Slides approximately 2 feet above ground
Transect set at 7 A.M.

Fig. 4.—Radial dispersion of *Ambrosia elatior* pollen.

As an example of converse behavior deviation, a radial dispersion study of *Albizzia lebbek* (woman's tongue) was made (Fig. 3). Albizzia belongs to the order Rosales, family Mimosaceae. This order is considered to be primarily insect pollinated, although the structure of the flowers of some of the Mimosaceae suggest the possibility of transition to anemophily.[58] In this area of Florida there have been reports of proved clinical cases of sensitization to Albizzia pollen.[62] An examination of the data presented in Fig. 3 may suggest a possible transition on the part of this species of Mimosaceae.

To recapitulate, Ambrosia, which is a notoriously heavy wind pollinator and primary cause of pollinosis in other parts of the United States, demonstrated what appeared to be a reversal in pollinating behavior. It has not been reported

to produce important clinical sensitization in this area. Albizzia, on the other hand, as a representative of an entomophilous family, apparently is transitional in the direction of anemophily. The fact that Albizzia has been reported to cause pollinosis in this area would indicate wind pollination under certain circumstances.

It should not be considered that these limited studies on dispersal are sufficient basis for any valid conclusions; but a comparison of these two examples illustrates the necessity for adapting pollen analysis methods, in a particular region, to significant environmental factors. The necessity of complete ecologic studies becomes obvious when an examination is made of two instances of behavior deviation.

The compilation of chronologic, meteorologic, and identification materials, the influence of meteorologic factors on air-load of pollens, and a suggested method of determining dispersion of pollens are presented as reference materials and as suggestions for further investigation. This preliminary investigation has brought sharply into focus the necessity of botanical field observations as a foundation for aerobiologic studies with reference to pollens.

LIST OF COMMON NAMES OF PLANTS IN FIG. 1.

Acer rubrum—Red maple
Acrostichum—Strap ferm
Albizzia lebbek—Woman's tongue
Amaranthus spinosus—Spiny amaranth
Ambrosia elatior—Short ragweed
Andropogon halipensis—Bunch grass, broom grass
Atriplex sp.—Salt-bush
Capriola dactylon—Bermuda grass
Casuarina sp.—Australian pine
Chenopodium album—Lamb's quarters
Chenopodium ambrosioides—Pig weed
Chrysobalanus icaco—Cocoa plum
Coccolobis uvifera—Sea grape
Cocos nucifera—Coconut palm
Conocarpus erecta—Buttonwood
Dipholis salicifolia—Bustic
Eleocharis sp.—Spike rushes
Ilex cassine—Dahoon, yaupon
Iva imbricata—Marsh elder
Laguncularia racemosa—White mangrove
Mangifera sp.—Mango
Mariscus jamaicensis—Saw-grass
Melaleuca leucodendron—Cajeput, bottle brush tree
Myrica cerifera—Wax myrtle
Ocotea catesbyana—Lancewood
Panicum sp.—Witch grass
Persea americana—Avocado
Pinus caribbaea—Slash, Caribbean pine
Pinus clausa—Sand pine
Pithecolobium sp.—Cat's-claw, black-bead tree
Quercus sp.—Oaks
Rapanea guayanensis—Myrsine, marlberry
Roystonea regia—Royal palm
Ruppia maritima—Sea grass
Sabal palmetto—Cabbage palm
Salix amphibia—Florida willow
Serenoa repens—Saw palmetto
Solidago sp.—Goldenrods
Tamala borbonii—Red bay
Tamarindas indica—Tamarind
Taxodium sp.—Cypress
Trema floridana—Florida Trema
Tricholaena rosea—Natal grass
Typha sp.—Cat-tail
Zamia floridana—Coontie, Florida arrowroot

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HEADACHE STUDIES. STATISTICAL DATA. I. PROCEDURE AND SAMPLE DISTRIBUTION

HENRY D. OGDEN, M.D.,* NEW ORLEANS, LA.

IN 1946 I became especially interested in the problem of headache. I found that headaches were often associated with nasal allergy, and that in these patients the nasal symptoms could be either prominent or extremely mild in degree. I previously reported a small series of cases that were associated with nasal blockage and who also had a background of sensitization to house dust.[1] Headaches could be precipitated by overdosage with house dust extract, and the patients were helped by treatment. This indicated a connection which I felt should be amplified and further studied. The literature was not too helpful, and no reports on large group studies of headache types were available. It has not been generally recognized that many physicians have had to rely on headache statistics that are based on either small studies, or on groups of patients. Studies on small groups are not statistically significant. Studies on patients provide figures which are true for sick people only, and cannot be interpreted as true for the general population. A worker may quote a certain figure which is requoted again and again, and finally becomes an established fact; however, the statistical reliability of the original figures was insufficient to warrant their conclusions.

An excellent study of headache was made by Fothergill in 1778.[2] He recognized certain headache patterns, and the relation of headache to various factors. He emphasized the importance of frontal headache but his conclusions have not been well remembered. It is interesting to note how closely some of Fothergill's observations are herein confirmed statistically. It is also surprising to note the fact that such a common complaint as headache has been allowed to rest on imperfect evidence from the standpoint of large group studies.

In a pilot study involving 251 office patients with respiratory allergy, I found that 58 per cent had sufficient frontal headaches to warrant complaint and discussion, wheras in a control group of 100 young adult individuals with no symptoms, the incidence of frontal headache was only 27 per cent. Anyone with nasal symptoms or frequent colds was excluded from the control group.

This problem obviously warranted further study. Sandoz Pharmaceuticals furnished a grant to the L.S.U. School of Medicine which made it possible to begin planning this study in early 1949.

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*From the Department of Medicine, Louisiana State University School of Medicine, New Orleans, La.

It was recognized that sampling the population at random would not give accurate figures, therefore, throughout the survey, 95 per cent cooperation of any group surveyed was deemed essential. This would give a crossection view of the group. Several groups that did not cooperate to this extent were discarded and the data not used. Nearly 6000 individuals were included in the gross sample, but only 4,634 satisfactorily cooperating individuals in groups are herewith reported.

In order to cross check accuracy, three separate surveying procedures were employed. We designated these groups as follows. Group I, the general group, consisted of heterogeneous individuals. These individuals consisted of employes of Charity, Southern Baptist, and Eye, Ear, Nose, and Throat hospitals in New Orleans. This obviously included various types of personnel, and would almost parallel the general adult employed population. Here the questionnaires were distributed and collected through the direct help of management.

Then, in order to determine whether there would be any great difference between answers of this type and those obtained by interviewers, it was arranged to personally interview several diverse categories of individuals. This part of the survey is designated as Group II. These individuals were homogeneous in their various classes, and included salesmen, saleswomen,* housewives, white manual laborers,* and Negro manual laborers.*

Group III consisted of five separate classes of individuals whose intelligence was of high enough level, so that accurate responses could be anticipated without interviewing. This included freshmen medical students, senior medical students, physicians, white and Negro Catholic Sisters.*

Group IV was simply the total of these previously mentioned groups.

It will be seen that comparable findings in different groups adequately paralleled each other in almost all instances. This fact indicates that each of the methods of study provided reliable data.

Questionnaires were sent to New York where the findings were transposed to IBM cards. After this was done, calculations and computations could be made on virtually any combination or relationship desired. Incidentally, the data reported herein represent only a part of the virtually infinite number of relationships which is possible to obtain.

The questionaire shows the extent and the simplicity of the survey. Other questions could have been asked, but an arbitrary limit had to be set, so that it would not get too complicated or lengthy. This final form is a revised one, after a test study had been made using a questionnaire which we found unsatisfactory. The data from this test study were discarded.

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*Through the cooperation of the Sewerage & Water Board of the City of New Orleans, we were able to interview laborers engaged strictly in heavy outdoor manual labor. Even foremen and supervisors were excluded. These men are to be distinguished from those classified as manual workers in Group I where the manual classification includes those doing menial tasks as well as strenuous labor. The salesmen and saleswomen were employees in the D. H. Holmes Department Store.

The cooperation of the Roman Catholic Archdiocese of New Orleans made possible the survey of religious groups.

It is noteworthy that excellent cooperation was obtained from employers and employees in New Orleans. On the other hand, several attempts to cross check this study in Metropolitan New York City met with insufficient cooperation to furnish statistical significance, even though employers gave their support.

HEADACHE SURVEY

No.

PLEASE FILL THIS OUT WHETHER YOU HAVE HEADACHES OR NOT AND PLEASE RETURN WITHIN THREE DAYS.

.....MANY THANKS. This survey is being made in order to determine the percentage and types of headaches existing in different groups of people. The information which you supplied is confidential and will be used for scientific statistical data only. Your cooperation is deeply appreciated.

Allergist, Department of Medicine
L.S.U. School of Medicine
New Orleans, Louisiana

INSTRUCTIONS

1. Mark "X" in the space provided unless otherwise requested.
2. Where information is requested, be accurate and BRIEF.
3. Many questions have more than one answer... In such cases mark an "X" by EACH answer which applies.
4. Please fill out COMPLETELY... Don't stop half way through.
5. Name and address may be omitted if preferred.

Name: _____ Address: _____

City: State: Date:

SEX	"X"
1 Male	
2 Female	

RACE	"X"
1 White	
2 Negro	
3 Oriental	
4 Indian	
5 Mixed	

MARITAL STATUS	"X"
1 Single	
2 Married	
3 Separated	
4 Divorced	
5 Widowed	
Age	

EDUCATION	"X"
1 College graduate	
2 College student	
3 High school grad.	
4 Grammar school grad.	
5 Partial gram. sch. ed.	
6 Trade school ed.	
0 None	

OCCUPATION	"X"
1 Agriculture	
2 Housewife	
3 Salesman	
4 Clerical	
5 Manual	
6 Executive	
7 Professional	
8 Student	
9 None	
10 Other (Name)	

GENERAL MEDICAL INFORMATION

A. Are you often or regularly troubled with.....	"X"
1 Hay fever?	
2 Running nose?	
3 Sneezing spells?	
4 Itching of nose or eyes?	
5 Discharge from nose?	
6 Discharge from eyes?	
7 Blocked nose?	
8 Drip in back of throat?	
9 Sinus trouble?	
0 Not troubled with any above	

B. Is there any asthma, hay fever, chronic nose trouble, hives, eczema, or other allergy in your blood relatives? (parents, grandparents, aunts, uncles, brothers, sisters.)	"X"
0 No	
1 Yes	

C. Do you have...	"X"
1 Asthma or wheezing?	
2 Repeated coughs?	
3 Frequent sore throats?	
4 Phlegm in throat?	
0 Do not have any of above	

D. Do you...	"X"
1 Smoke usually?	
0 Smoke rarely or never?	

E. Do you...	"X"
1 Use nose drops usually?	
2 Use drops during colds?	
0 Never use nose drops?	

F. Do you have colds	"X"
0 Never?	
1 One or two per year?	
2 Three to six per year?	
3 Almost constantly?	
4 Constantly?	

G. Do you ever have...	"X"
1 Hives?	
2 Eczema?	
3 Poison Ivy type of rash?	
0 None of above	

H. Are you exposed to any unusual substances in your work? "X"

0 No
1 Yes

If "yes", describe these below:

_____

_____

HEADACHE INFORMATION

A. Do you have headaches?	"X"
0 No	
1 Yes	
2 Formerly, but not now	

(If you USED to have headaches, but NO LONGER do, please FILL IN ALL questions as if you still had them.)

B. About how many headaches do you have? Per Month _____ or Per Year _____

C. Do any of your blood relatives suffer regularly from headaches? "X"

0 No
1 Yes

D. Do your headaches come:	"X"
1 Mostly in the spring?	
2 Mostly in the summer?	
3 Mostly in the autumn?	
4 Mostly in the winter?	
5 At no particular season?	

E. Which part of your head may be in pain during most headache attacks?	Mark an "X" by: EACH part in pain	Mark an "X" by: the ONE part most OFTEN painful
1 Forehead one side only		
2 Forehead both sides		
3 Whole front of head		
4 One side of head only		
5 Both sides of head		
6 Top of head		
7 Back of head		
8 Neck		
9 Face		
10 Eyes		
11 Bridge of nose		
12 ALL OVER the head		

13 Remarks

_____

_____

_____

HEADACHE SYMPTOMS EXPERIENCED

			"X"
A.	Can you tell when a headache is approaching?		
	If yes, describe how?	0 No	
		1 Yes	

B.	Is your vision disturbed...	"X"
1	Before headaches?	
2	During headaches?	
3	Both before and during?	
0	Not at all?	

C.	During headaches do you...	"X"
1	Usually vomit?	
2	Occasionally vomit?	
3	Get nauseated? (sick at stomach)	
0	Never vomit nor get nauseated?	

D.	What time of the day do your headaches usually appear?	"X"
1	On awakening?	
2	Forenoon?	
3	Afternoon?	
4	Evening?	
5	After work?	
6	During sleep?	
0	No particular time?	

E.	Do you experience the following?		"X"
1	Trouble with nose BEFORE OR DURING headaches?		
2	Neck pains DURING headaches?		
3	Neck pains BEFORE OR AFTER headaches?		
4	Muscular pains DURING headaches?		
5	Muscular pains AFTER headaches?		
6	"Tingling, or	BEFORE headaches?	
7	changes of	DURING headaches?	
8	sensation"	AFTER headaches?	
9	Muscular weakness during attacks?		
10	Ringing of ears during headaches?		
0	None of above?		

F.	How long do MOST of the headache attacks last?	"X"
1	LESS than one hour?	
2	1 to 6 hours?	
3	6 to 12 hours?	
4	12 to 24 hours?	
5	1 to 2 days?	
6	3 days or longer?	

G.	Do the headache pains...	"X"
1	Feel sharp and stabbing?	
2	Feel dull and pressure-like?	
3	Feel throbbing?	
4	Remain constant?	
5	Change during the attack?	

SUSPECTED CAUSES

"X" any of the below listed causes which you think bring on your headaches:

1	Fatigue or being tired		6	Overeating		11	Menstruation	
2	Allergy to some subs. or food		7	Over-drinking		12	Emotions	
3	Colds, or respir. infect.		8	Overheating		13	Worry	
4	Too much smoking		9	Sinus trouble		14	Constipation	
5	Eye strain		10	Change of life		15	Getting chilled	
17	Others: (Describe here): _____					16	Exercise	
						0	Have no idea of cause	

HEADACHE TREATMENT

	Do any of the following medicines help your headache?			"X"
A.	Simple remedies such as aspirin, Anacin, B-C, Stanback, etc.	0	No	
		1	Yes	
		2	Sometimes	
		3	Never tried	
B.	Stronger narcotic drugs, such as codeine, etc.	0	No	
		1	Yes	
		2	Sometimes	
		3	Never tried	
C.	ERGOTAMINE drugs such as Gynergen, DHE-45, Cafergone, etc.	0	No	
		1	Yes	
		2	Sometimes	
		3	Never tried	
D.	Tablets for allergy (Antihistaminics such as Benadryl, Pyrabenzamine, Pyrrolozote, etc.	0	No	
		1	Yes	
		2	Sometimes	
		3	Never tried	
E.	Nose drops	0	No	
		1	Yes	
		2	Sometimes	
		3	Never tried	

F.	Which medicines do you prefer for your headaches?	"X"
1	Aspirin, Anacin, B-C, Stanback, etc.	
2	Codeine, etc.	
3	Gynergen	
4	DHE-45	
5	Cafergone	
6	Antihistaminics	
7	Nose drops	
0	None at all	
	List others here	

G.	Is the treatment of your headaches being directed by any of the following?	"X"
1	Ear, Nose and Throat specialist?	
2	Eye specialist?	
3	Allergist?	
4	Neuropsychiatrist?	
5	Neurosurgeon?	
6	Specialist in internal medicine?	
7	Physician not specializing in any of the above?	
8	Dentist?	
0	No one at all?	
	List others here:	

We further divided each group into headache and nonheadache fractions. It should be remembered that all types of headache are included in this study. In the tables wherever per cents do not add to 100, the difference indicates the number who did not answer the particular question.

TABLE I. DISTRIBUTION OF SAMPLE

GROUP	I	II	III	IV
Total cases	3589	501	544	4634
Male	22.2%	60.1%	55.7%	30.2%
Female	77.8%	39.9%	44.3%	69.8%
White	66.2%	79.8%	86.0%	70.0%
Negro, etc.	33.4%	20.2%	14.0%	29.7%
No. headaches	2380	205	420	3005
% headaches	66.3%	40.9%	77.3%	64.8%

This shows the percentage distribution and makeup of the survey. Tables I, II, and III are not weighted and are included in order to describe the survey composition. It is seen that in 4,634 individuals, the percentage of all types of headache is almost 65 per cent. In Table II we see that the executive group was very small and that the agricultural group was too small to furnish any information.

TABLE II. SAMPLE DISTRIBUTION (PER CENT)

GROUP	I	II	III	IV
Married	40.7	75.2	29.2	43.1
Single	37.5	13.8	70.8	38.9
Widowed	10.4	4.4	0	8.5
Separated	5.9	2.2	0	4.8
Divorced	5.1	3.8	0	4.3
Manual	44.1	39.9	0	38.5
Professional	21.6	0	59.4	23.7
Student	8.9	0	40.4	11.7
Housewife	11.0	19.9	0	10.7
Clerical	13.0	0	0	10.0
Salesman	0.1	39.9	0	4.4
Executive	0.6	0	0.2	0.5
Agriculture	0.2	0	0	0.1

Tables IV, V, VI, VII show the distribution of groups according to headache and nonheadache fractions.

In Table VI it can be seen that a significantly larger proportion of persons without headaches report no evidence of nasal complaints than do persons with headaches. This is also true for chest and throat complaints, and for "colds." These data were shown to be significant by Dr. Huldah Bancroft, Professor of Biostatistics, Tulane University School of Medicine. A statistically significant difference indicates, that in each of the above cases, such a difference between proportions would occur by chance alone less than once in one thousand times, i.e., $P = <0.001$. The probability of error was often infinitesimal. It is also interesting to note that in the total sample (Group IV) a considerably higher inci-

TABLE III. SAMPLE DISTRIBUTION (PER CENT)

	I	II	III	IV
College graduate	8.5	8.6	67.5	15.5
College student	10.8	8.6	23.2	12.0
High school graduate	39.3	29.5	3.7	34.0
Grammar school graduate	25.5	18.0	3.9	22.1
Part. grammar school	10.1	30.3	0.9	11.2
Trade school education	1.8	1.0	0.1	1.5
Uneducated	4.0	4.0	0.6	3.7
Age to 20 years	12.4	1.0	9.7	10.8
21-30 years	31.2	30.9	46.1	32.9
31-40 years	20.0	26.1	14.0	20.0
41-50 years	19.0	25.1	14.7	19.2
51-60 years	12.2	13.2	6.3	11.6
61 years or older	5.2	3.7	4.2	4.9

TABLE IV. DISTRIBUTION OF SAMPLE

	I		II		III		IV	
	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE
Total number	2380	1209	205	296	420	124	3005	1629
Male	17.4	31.6	36.6	76.4	52.6	66.1	23.6	42.4
Female	82.6	68.3	63.4	23.6	47.4	33.9	76.4	57.6
White	65.8	67.0	96.1	68.6	83.8	93.5	70.3	69.3
Negro, etc.	33.8	33.0	3.9	31.4	16.2	6.5	29.3	30.6
College graduate	9.0	7.5	9.8	7.8	64.1	79.0	16.8	13.0
College student	12.3	7.9	14.1	4.7	25.7	14.5	14.3	7.8
High school graduate	42.3	33.3	41.0	21.6	4.3	1.6	36.9	28.8
Grammar school graduate	23.8	28.9	21.0	15.9	4.0	3.2	20.8	24.6
Part grammar school education	8.4	13.4	12.2	42.9	1.0	0.8	7.6	17.8
Trade school education	1.6	2.1	1.4	6.4	0.2	0	1.4	1.7
None	2.6	6.9	0.5	0.7	0.5	0.9	2.2	6.3

TABLE V. DISTRIBUTION OF SAMPLE

	I		II		III		IV	
	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE
Single	39.4	33.8	11.7	15.2	74.5	58.1	42.4	32.2
Married	40.3	41.4	74.6	75.7	25.5	41.9	40.6	47.6
Separated	6.5	4.8	1.4	2.7	0	0	5.3	4.1
Divorced	5.3	4.6	5.9	2.4	0	0	4.6	3.9
Widowed	8.2	14.8	5.9	3.3	0	0	6.8	11.6
Agricultural	0.1	0.2	0	0	0	0	0.1	0.2
Housewife	11.8	9.3	30.7	12.5	0	0	11.5	9.1
Salesman	0.1	0.2	57.6	27.7	0	0	4.0	5.2
Clerical	13.4	12.2	0	0	0	0	10.6	9.1
Manual	40.2	51.8	11.7	59.5	0	0	32.6	49.2
Executive	0.7	0.4	0	0	0.2	0	0.6	0.3
Professional	23.0	18.9	0	0	54.8	75.0	25.9	19.7
Student	10.3	6.3	0	0	45.0	25.0	14.4	6.6
Age to 20	14.6	7.9	0.5	1.4	11.0	5.6	13.1	6.6
21-30	35.6	22.4	34.1	28.7	52.1	25.8	37.8	23.8
31-40	21.3	17.5	28.3	24.7	12.1	20.2	20.5	19.0
41-50	17.1	22.8	28.3	23.0	11.9	24.2	17.1	23.0
51-60	9.1	18.4	8.3	16.6	5.0	10.5	8.5	17.4
Over 60	2.3	11.0	0.5	5.6	2.4	10.5	2.2	9.9

TABLE VI. DISTRIBUTION OF SAMPLE

	I		II		III		IV	
	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE
Hay fever	9.4	6.0	14.6	7.4	14.0	12.9	10.4	6.8
Running nose	6.6	3.1	14.1	5.7	11.2	5.6	7.8	3.8
Sneezing spells	12.5	5.0	17.1	7.4	17.1	8.1	13.5	5.7
Itching nose, eyes	11.5	3.6	14.1	4.4	13.1	8.1	11.9	4.1
Disch. from nose	4.2	2.2	11.7	5.1	11.4	5.6	5.7	3.0
Disch. from eyes	3.3	1.6	5.4	3.4	4.8	3.2	3.7	2.0
Blocked nose	10.8	2.6	19.5	5.1	24.4	12.1	13.3	3.8
Drip back of throat	15.3	4.2	18.0	3.7	31.7	15.3	17.8	5.0
Sinus trouble	13.6	2.8	19.5	5.1	20.2	8.1	14.9	3.6
None of above	57.9	82.3	55.6	84.1	39.0	62.9	55.1●	81.2●
Asthma or wheezing	3.4	2.3	2.4	2.7	4.8	4.8	3.5	2.6
Repeated coughs	5.1	2.2	5.4	2.4	6.9	4.0	5.4	2.4
Freq. sore throats	9.5	2.5	6.3	1.0	13.6	3.2	9.8	2.3
Phlegm in throat	12.7	4.1	13.2	2.4	30.7	16.1	15.2	4.7
None of above	74.5	86.7	77.6	89.9	56.0	75.8	72.1●	86.4●
No colds	8.3	25.7	9.2	16.2	4.0	17.7	7.8●	23.4●
One or two/yr.	71.8	61.7	74.6	76.4	58.6	65.3	70.2	64.6
Three to six/yr.	15.8	5.6	12.7	7.4	31.9	15.3	17.9	6.7
Almost constantly	3.2	1.2	1.5	0	5.2	1.7	3.3	1.0
Constantly	0.9	0.6	2.0	0	0.3	0	0.8	0.4

●Tested by Dr. Huldah Bancroft and was found to be statistically significant.
:Tested by Dr. Huldah Bancroft and was *not* found to be statistically significant.
This key applies to subsequent tables and illustrations

TABLE VII. DISTRIBUTION OF SAMPLE

	I		II		III		IV	
	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE	HEAD-ACHE	NON-HEAD-ACHE
Use nose drops usually	6.1	2.1	9.3	2.0	6.4	0.8	6.3	2.0
Use during colds	42.4	18.5	41.0	24.7	34.8	29.8	41.3	20.5
Never use drops	51.5	74.8	49.7	73.3	58.8	69.4	52.4	74.1
Smoke usually	35.0	29.9	56.1	65.2	31.4	32.3	35.9	36.5
Smoke rarely or never	65.0	65.8	43.9	34.8	68.6	67.7	64.1	60.3
Hives	6.2	3.1	12.7	4.4	9.5	7.3	7.1:	3.7:
Eczema	2.0	0.9	2.9	1.7	4.3	0	2.4	1.0
Poison ivy	4.1	1.9	6.3	5.4	9.5	4.8	5.0	2.8
None	88.1	87.8	81.0	89.9	80.0	87.9	86.5	88.2
Unusual exposures	17.5	10.9	6.8	1.4	13.6	8.1	16.2	9.0
None	82.5	80.0	93.2	98.3	86.4	91.9	83.8	84.2
Allergy in family	22.2	9.7	22.9	8.8	42.9	33.1	25.1●	11.3●
None	77.8	86.7	77.1	91.2	57.1	66.9	74.9	86.0

dence of each respiratory symptom, without exception, occurred in the headache fraction. In Table VII, hives, eczema, and poison ivy were reported approximately twice as often in the headache fraction of the total group in comparison to the nonheadache fraction. The proportion of cases with hives in the headache group when compared with that in the nonheadache (7.1 vs. 3.7) did not show a significant difference because of the small percentages involved. However, the trend is obvious. Nose drops were used about twice as much in the headache

TABLE VIII. DISTRIBUTION OF HEADACHE FRACTION

	I	II	III	IV
1-6 per year	27.4	24.3	20.7	26.1
7-12 per year	26.4	28.7	22.1	26.0
13-24 per year	17.6	14.4	16.4	17.2
25-48 per year	16.5	6.9	19.3	16.1
49-96 per year	6.1	12.4	10.2	7.3
97-360 per year	5.9	13.4	11.3	7.4
Headaches in family	27.6	28.3	37.2	28.9
None	72.2	71.7	62.6	70.9
Mostly in spring	2.9	2.9	1.4	2.7
Mostly in summer	7.8	12.7	4.8	7.7
Mostly in autumn	0.6	2.0	1.9	0.9
Mostly in winter	3.9	4.4	8.8	4.7
No particular season	80.5	79.0	83.3	80.8

TABLE IX. DISTRIBUTION OF HEADACHE FRACTION

LOCATION OF HEADACHE	I		II		III		IV	
	EACH	MOST OFTEN	EACH	MOST OFTEN	EACH	MOST OFTEN	EACH	MOST OFTEN
Forehead—1 side	12.5	13.7	12.5	11.2	12.6	11.4	12.3	13.0
Forehead—both	25.8	20.0	57.8	43.6	31.5	22.8	28.0	22.7
Whole fr. head	27.3	22.1	16.8	9.3	28.6	16.7	26.6	20.0
One side head	6.6	5.5	3.1	0.6	9.5	8.4	6.7	5.6
Both sides head	5.4	3.6	8.0	3.1	8.2	3.6	5.9	3.5
Top of head	11.0	7.0	9.9	3.1	11.1	6.0	10.7	6.5
Back of head	12.9	8.2	26.8	14.3	21.8	10.0	14.8	9.1
Neck	6.4	1.3	9.3	3.7	7.5	1.7	6.6	1.6
Face	1.6	.8	5.6	1.9	1.9	.7	1.8	0.9
Eyes	23.2	13.1	18.0	8.7	25.9	13.1	22.9	12.6
Nose bridge	4.5	4.6	1.9	0.6	5.6	5.6	4.5	4.4
Entire head	10.1	0	13.0	0	15.0	0	10.8	0
No answer	4.2	47.5	21.5	21.5	1.7	28.8	3.6	43.1

TABLE X. DISTRIBUTION OF HEADACHE FRACTION

	I	II	III	IV
Prodrome	19.6	29.3	24.0	20.9
None	79.6	70.7	74.5	78.3
Visual disturbance before	3.0	2.4	1.9	2.8
Visual disturbance during	19.8	15.1	23.3	20.0
Both before and during	6.2	3.9	7.2	6.1
None	70.2	78.1	66.2	70.2
Usually on awakening	12.8	13.2	16.2	13.3
Forenoon	3.4	4.4	2.9	3.4
Afternoon	8.6	12.7	18.1	10.2
Evening	6.1	8.3	15.5	7.6
After work	7.0	6.3	8.3	7.1
During sleep	1.9	0	2.4	1.9
No particular time	64.9	59.0	47.6	62.1
Less than 1 hour	31.1	27.8	17.6	28.9
1-6 hours	41.4	51.7	55.7	44.1
6-12 hours	5.3	6.8	8.6	5.9
12-24 hours	2.9	5.4	1.9	2.9
1-2 days	6.5	4.9	5.0	6.2
3 days or longer	2.9	2.4	3.3	2.9
No answer	9.9	1.0	7.9	9.1

fraction. The proportion in the total sample showing a family history of allergy is significantly higher among persons having headaches than among those not having headaches. This finding was consistent in all groups.

In Table VIII the frequency of headache in different groups is evaluated; 48.0 per cent of the total have more than one headache a month; 30.8 per cent have more than 2 headaches a month. It was also observed that over 1 per cent of the total have daily headaches.

We can see that there is a known family history of headache in 29 per cent of all individuals reporting headaches themselves.

There is no clear-cut seasonal incidence of headache.

PERCENTAGE OF HEADACHE ACCORDING TO SEX

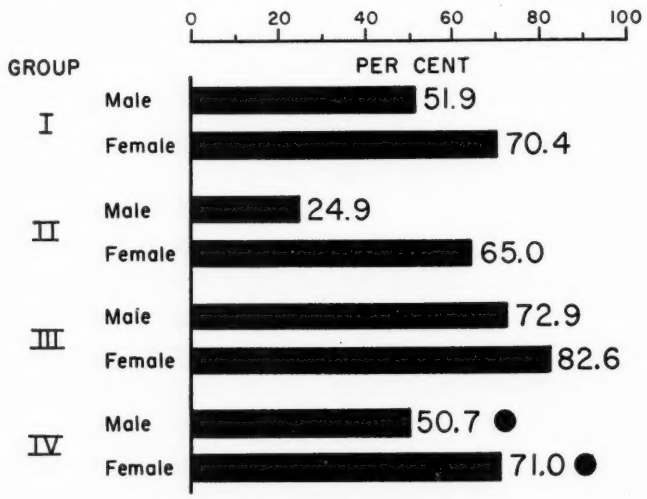

Fig. 1.

In Table IX we have a tabulation of the sites of head pain as reported by the individuals. It is obvious that pain predominates in the forehead, either on one or both sides or in the region of the eyes. We can call this, therefore, the frontal type of head pain. It should be pointed out that these figures are based on the number who answered the questions.

Of all headache patients (Table X), 78.3 per cent report no prodromal symptoms; 70.2 per cent of the sample reported no visual disturbances. However 20 per cent had visual difficulty during headaches. No particular time of day for the onset of headache was reported by 62.1 per cent of the patients. However, 13.3 per cent report headaches on awakening, and 10.2 per cent report headaches appearing in the afternoon.

The presence of nasal symptoms (Table XI) was associated with the onset of headache in 7.9 per cent of the individuals. Neck pains are frequently present

during attacks. Over 70 per cent of individuals report no nausea or vomiting with headache, while 20.9 per cent report nausea. It is also seen that most headaches are considered to be dull and pressure like in nature. The throbbing type is next in order of frequency.

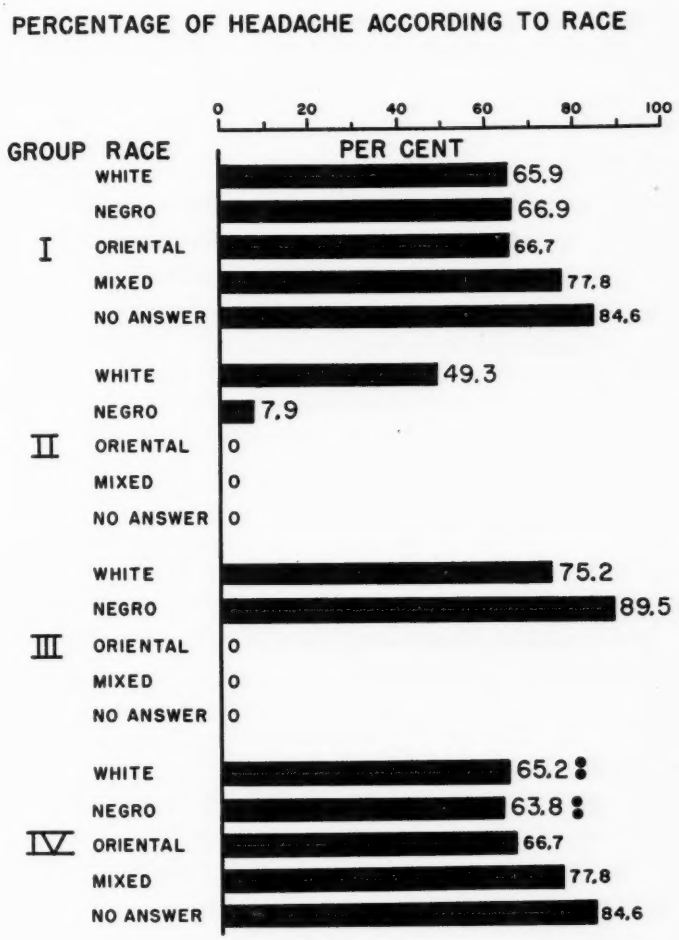

Fig. 2.

Table XII lists suspected causes of headache. Fatigue and eyestrain are most commonly blamed. Menstruation is blamed by 31.1 per cent of women.

Table XIII shows results obtained with different types of symptomatic treatment, and it is obvious that many headache sufferers have not used all of these different types of remedies. As an example many individuals have never used an antihistaminic in the treatment of headache. In this table the Group II figures differ very markedly from those of the other groups. We feel that in this personally interviewed group, the question was correctly interpreted, whereas in Groups I and III, many individuals apparently reported "no" when they

TABLE XI. DISTRIBUTION OF HEADACHE FRACTION

	I	II	III	IV
Nasal symptoms before or during	6.8	7.8	13.6	7.9
Neck pains during	14.2	15.1	16.9	14.7
Neck pains before or after	2.5	4.4	4.3	2.9
Muscular pains during	4.8	6.3	5.7	5.1
Muscular pains after	1.6	1.0	1.2	1.5
Paresthesias before	1.1	1.0	1.9	1.2
Paresthesias during	2.8	2.4	3.8	2.9
Paresthesias after	0.8	0.5	0	.7
Muscular weakness during	4.3	8.3	3.6	4.5
Tinnitus	6.3	7.3	7.6	6.5
None	69.0	67.3	59.5	67.6
Usually vomit	2.0	2.0	1.4	1.9
Occasionally vomit	5.1	6.8	5.5	5.3
Get nauseated	21.1	19.0	21.0	20.9
Neither	71.0	72.2	70.7	71.1
Sharp and stabbing	11.8	12.2	11.4	11.8
Dull and pressurelike	34.5	55.6	47.4	37.7
Throbbing	28.6	31.7	35.5	29.8
Constant	16.3	14.6	18.6	16.5
Change during attack	8.1	8.3	6.9	8.0
No answer	14.1	2.0	5.5	12.0

TABLE XII. DISTRIBUTION OF HEADACHE FRACTION SUSPECTED CAUSES

	I	II	III	IV
Fatigue	31.5	27.8	40.7	32.5
Allergy	4.3	6.3	6.2	4.7
Colds	11.4	5.9	22.1	12.5
Too much smoking	4.8	5.9	10.0	5.6
Eye strain	34.1	31.7	42.6	35.1
Overeating	1.9	2.9	1.7	1.9
Overdrinking	3.1	6.3	10.5	4.4
Overheating	7.0	5.4	4.3	6.5
Sinus trouble	10.8	14.6	15.2	11.6
Menopause	4.2	7.3	4.3	4.4
Menstruation	25.6	23.4	13.3	23.8
Emotions	9.8	19.5	10.7	10.6
Worry	13.0	15.6	15.2	13.5
Constipation	16.7	11.2	19.5	16.7
Getting chilled	1.6	1.0	0.7	1.4
Exercise	1.4	0	4.0	1.7
No idea of cause	13.4	9.3	7.1	12.2
Others	0	10.7	1.0	3.1
No answer	0.9	0	1.4	.9

should have reported "never tried." Therefore, in this respect, the results stated for Group II are probably fairly correct. The terms "no" and "never tried" were probably synonymous to many people in the other groups. This is corroborated by the fact that the narcotic drugs, and the Ergotamine drugs are only obtainable by prescription. Such a large number of people, as reported negative results with narcotics and the Ergotamines in Groups I and III, could hardly have used them. In the next table, we will see that 82 per cent of the total of the headache fraction are not being treated specifically for headache by any kind of physician. Therefore, the figures differentiating "no" and "never tried" in Group II of Table XIII are acceptable, whereas those in Groups I and III and therefore IV also, are probably unacceptable.

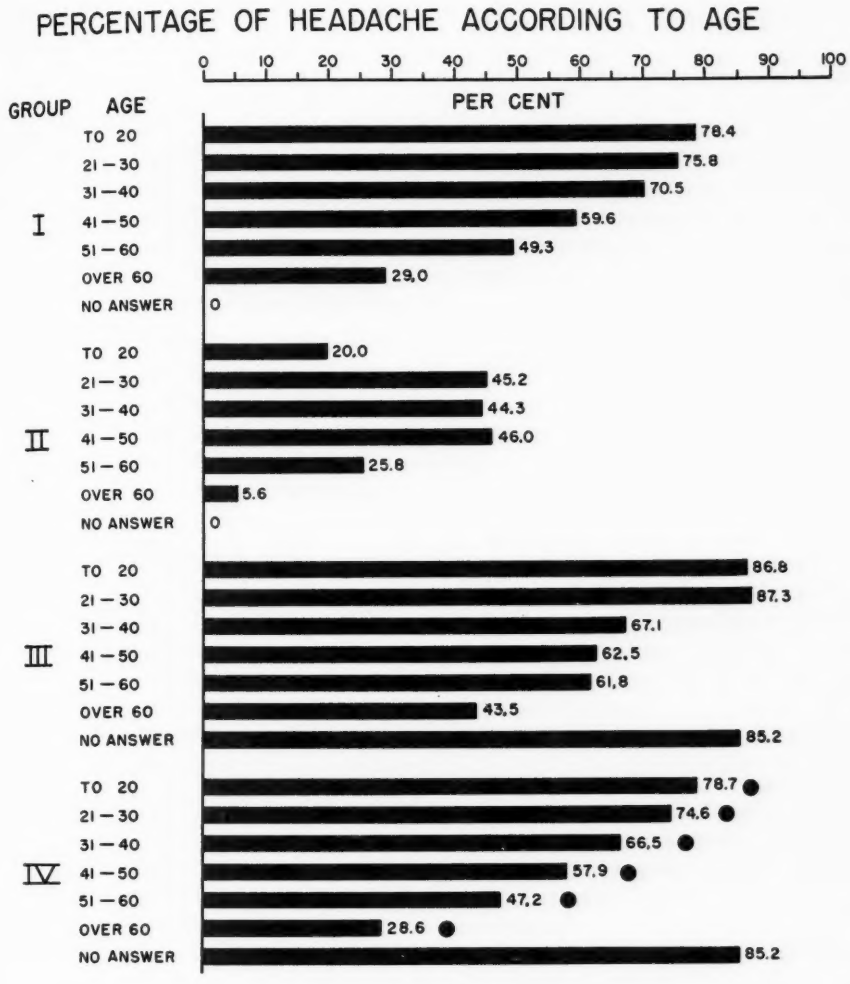

Fig. 3.

Table XIV shows that simple remedies such as aspirin are preferred by most individuals. However, it should be remembered that many headaches are mild, self-diagnosed, and self-treated. Hence, it follows that the most advertised products would be most widely used. The patient may not be driven to seek specific medical advice, unless the headaches become recurrent, more severe, and nonresponsive to simple medication.

Also in this table we report the types of therapist who are directing the treatment of headache sufferers. We see that the otorhinolaryngologists, ophthalmologists, and general practitioners are consulted most frequently.

In the next six charts the per cent of headache according to certain variations is presented. These figures are weighted; that is, they represent the per cent headache existing within the particular segment. In Fig. 1 we have the

TABLE XIII. DISTRIBUTION OF HEADACHE FRACTION

		TREATMENT			
		I	II	III	IV
Aspirin, etc.	No	9.5	6.3	7.6	9.0
	Yes	64.9	74.1	54.5	64.1
	Sometimes	21.1	13.7	30.3	21.9
	Never tried	3.6	5.4	6.2	4.1
Narcotics	No	40.9	2.0	22.9	35.7
	Yes	4.2	7.3	6.2	4.8
	Sometimes	2.4	1.5	2.6	2.3
	Never tried	51.6	88.7	66.9	56.3
Ergotamine group	No	41.8	1.0	24.8	35.9
	Yes	1.1	1.0	1.2	1.0
	Sometimes	0.7	0	0.5	.6
	Never tried	56.4	97.5	72.1	61.1
Antihistamine group	No	41.6	2.9	21.4	36.1
	Yes	3.2	2.4	4.8	3.4
	Sometimes	2.7	1.0	6.0	3.0
	Never tried	51.6	93.2	66.4	56.6
Nose drops	No	39.7	2.0	27.4	35.4
	Yes	6.7	5.4	6.4	6.6
	Sometimes	9.4	4.9	11.0	9.3
	Never tried	43.3	87.2	53.8	47.8

TABLE XIV. DISTRIBUTION OF HEADACHE FRACTION TREATMENT (CONTINUED)

	I	II	III	IV
Preferred treatment				
Aspirin, etc.	82.0	81.0	76.9	81.2
Narcotics	2.1	2.9	4.5	2.5
Gynergen	0.3	0.0	0.2	0.3
DHE-45	0.3	0.0	0.0	0.2
Cafergot	0.3	0.5	0.2	0.3
Antihistaminics	1.9	0.0	2.9	1.9
Nose drops	4.1	1.5	4.5	4.0
None at all	13.2	16.1	17.4	14.0
Treatment directed by				
E. N. T. specialist	4.7	2.9	6.4	4.8
Ophthalmologist	4.4	1.0	3.1	4.0
Allergist	0.5	0.5	1.9	0.7
Neuropsychiatrist	0.1	0.0	0.2	0.1
Neurosurgeon	0.1	0.5	0.0	0.1
Internist	2.4	1.5	1.2	2.2
Other physician	2.9	13.2	2.9	3.6
Dentist	0.8	0.0	0.0	0.7
No one	82.4	76.0	82.9	82.0

TABLE XV.

	Per Cent Headaches in Group II Components	
100	Salesmen	51.0
100	Saleswomen	67.0
101	White laborers	16.8
100	Negro laborers	8.0
100	Housewives	62.0
	Per Cent Headaches in Group III Components	
123	Freshman medical students	86.9
100	Senior medical students	85.0
95	Physicians	46.3
150	White Catholic sisters	80.0
76	Negro Catholic sisters	86.6

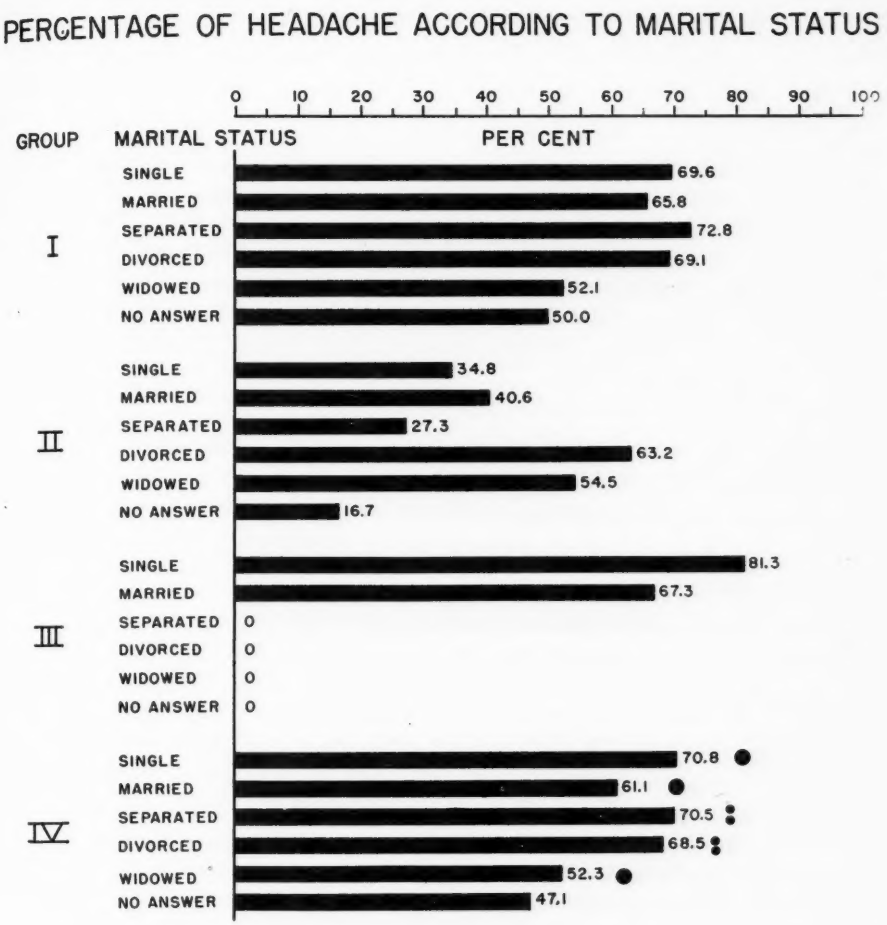

Fig. 4.

per cent of headache according to sex. We see that in the total or Group IV that 50.7 per cent of males have headaches, compared to 71 per cent of females. Dr. Bancroft finds that this difference is significant. The low percentage of headache in Group II males is due to the fact that two-thirds of the individuals were manual laborers, who, we see, have a markedly low incidence of headache.

In Fig. 2 we find that there is no significant difference according to race. The apparent discrepancy between the per cent of Negroes with headaches in Groups II and III is readily explainable. In Group II all the Negroes were male manual laborers of meager education, whereas in Group III, the Negroes consisted entirely of a female religious community, having an above average education. Group I, on the other hand, furnishes an ideal comparison between whites and Negroes since background factors were on a more comparable plane.

Other figures in Fig. 2 lack significance. There were only six (0.1 per cent) Orientals in the survey; there were only nine (0.3 per cent) who did not identify their race ("no answer").

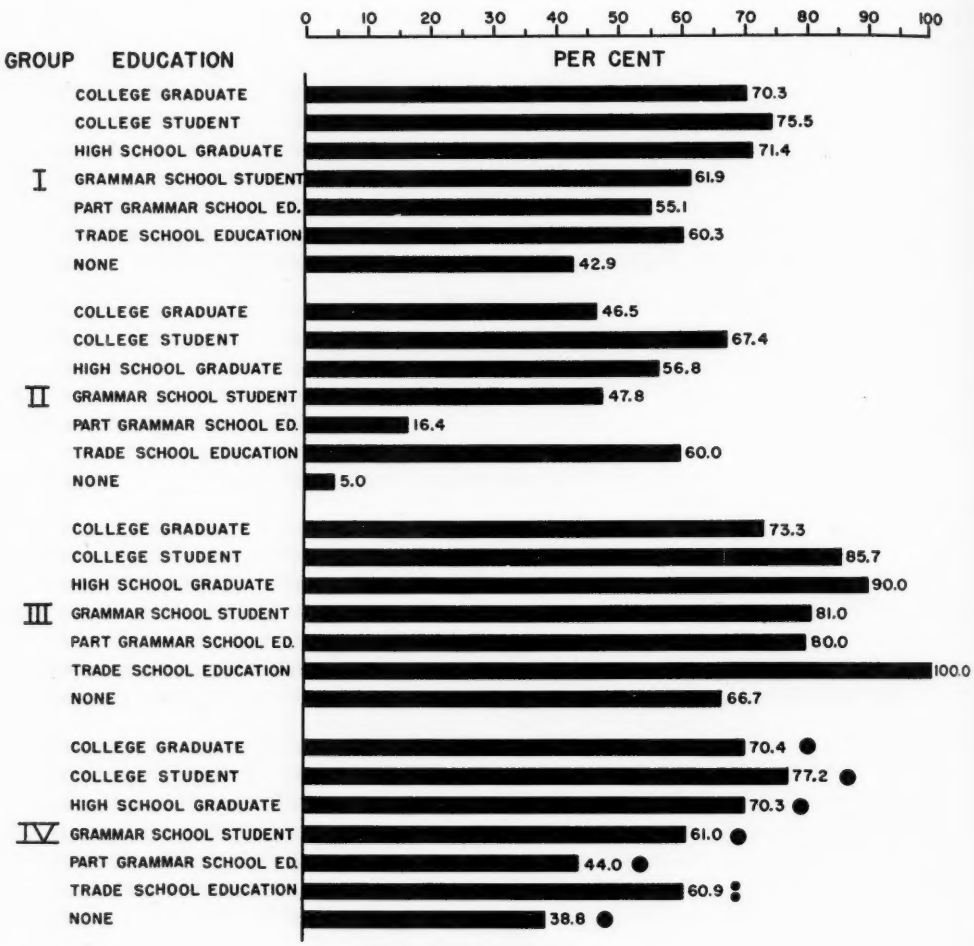

Fig. 5.

Fig. 3 shows that headaches decrease regularly with advancing age. This may be due to the vascular sclerosis that develops with age.

In Fig. 4 (Marital Status) we see that the proportion having headaches for single people was significantly higher, for married and widowed persons significantly lower, while the proportions of separated and divorced persons were not significantly different from the total group. Although the proportion having headache among separated and divorced persons was approximately the same as for single persons, the sample was too small to indicate that the difference was a real difference. It seems obvious however, that there are lesser headaches in individuals who are married when compared with those who are not presently in the married state. However, the marital state itself

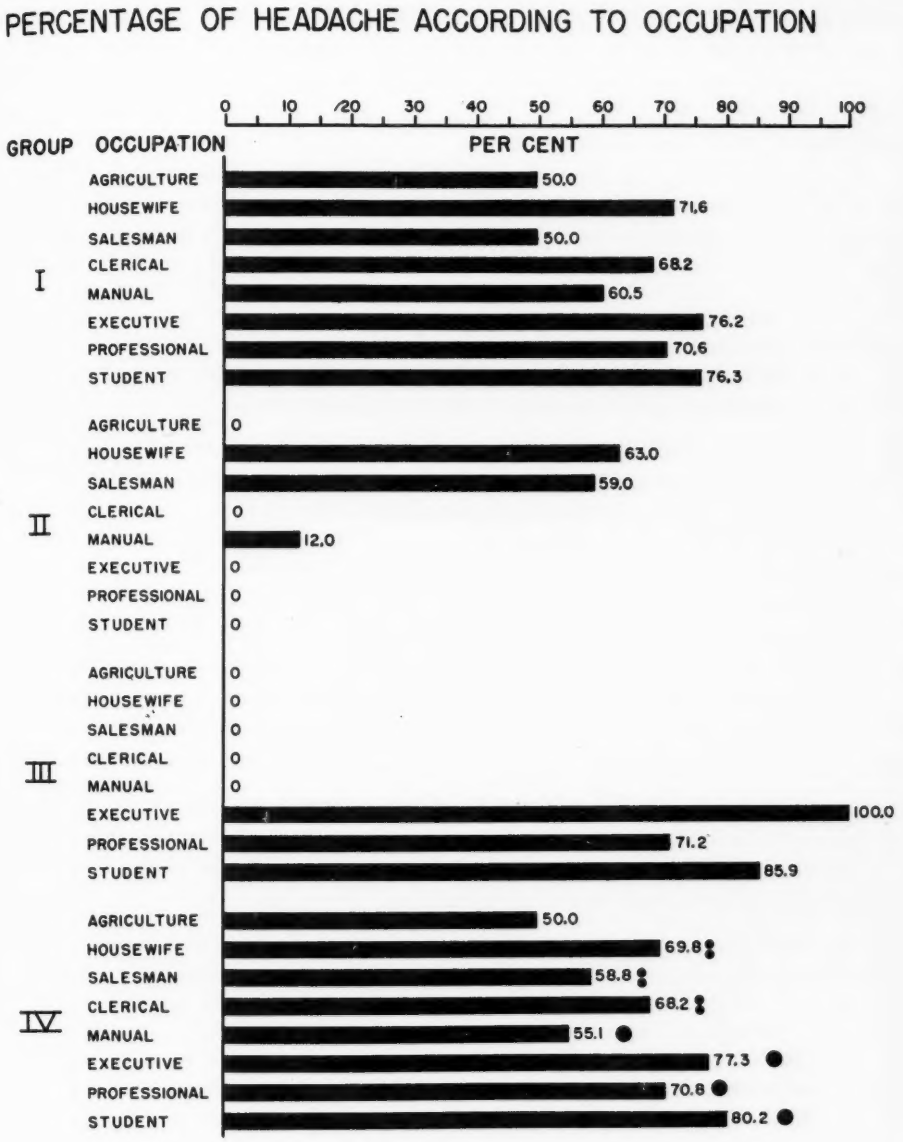

Fig. 6.

may not be the only important factor, since it must be remembered that single persons are generally younger than married ones. In the last chart we saw that younger people have more headaches. On the other hand, separated, divorced or widowed persons would not be predominantly young.

In Fig. 5 (Education) the proportions of college graduates, college students, high school graduates having headaches were significantly higher than the proportion for the group as a whole. The proportions for those having grammar school, partial grammar school education, and no education were

significantly lower. The proportion having a trade school education was not significantly different from the group as a whole (because of small numbers involved). Three individuals (out of 544) reported no education in Group III. This was obviously an error or a jest as this was a select group composed of educated individuals only.

From the standpoint of occupation (Fig. 6) there was a significantly higher proportion with headaches in the professional, student, and executive groups than in the general group. There was a significantly lower proportion for manual laborers, while the proportion of housewives, salesmen and clerical workers having headaches was not significantly different from the proportion for the total group.

Incidentally, the proportions of separate occupations in Group IV may not accurately mirror the general population makeup. On the other hand, Group I, as previously stated, more nearly approximates the general adult employed population.

Table XV gives the incidence of headache in components of Group II (personally interviewed) and Group III (highly intelligent individuals). The apparent discrepancy between the figure for housewives in Group II (62 per cent) and the figure for Fig. 6 (69.8 per cent) is based on the fact that many of the housewives (394) in Group I (hospital employees) had some other primary occupation. The student component of Group I included all types of students (grammar, nursing, etc.) whereas those in Group III were exclusively college students engaged in arduous mental activity. Incidentally in an incomplete study, the incidence of headaches in interns and residents was found to be approximately 65 per cent. This, of course, is roughly midway between that of medical students and physicians.

In another incomplete study, the incidence of headache among priests and lawyers was found to be approximately 65 per cent in each group.

SUMMARY

1. The incidence of headache of all types in 4,634 individuals was found to be 3,005 or 64.8 per cent.

2. Persons with headache have a higher incidence of various respiratory symptoms. These figures were shown to be statistically significant.

3. There is also a significantly higher familial history of allergy in these individuals.

4. Only 18 per cent of headache sufferers seek medical aid specifically for this complaint.

5. Pain in the frontal area constitutes the most frequent type of headache.

6. Headache incidence is greater among females, younger adults, single people, educated individuals, executives, students, and professional groups.

7. It is obvious therefore that there are several background factors to be considered in the management of headache. Proper recognition of the possible allergic basis may be very important, along with the handling of the mental, emotional, or occupational problems.

Acknowledgement is made of the assistance of Mr. James Villere, Southwest Manager of Sandoz Pharmaceuticals.

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PSYCHE AND ALLERGY

E. WITTKOWER, MONTREAL, CANADA

IN THE field of allergy harmony between psychiatrists and somaticists has often been lacking as in so many other fields of psychosomatic medicine. There are three main reasons for this disharmony; ignorance, prejudice, and technical jargon. Psychiatrists ignorant about allergic phenomena have not infrequently minimized their etiologic relevance just as allergists devoid of knowledge of psychopathologic mechanisms have disregarded or dismissed psychiatric findings; or if the existence of psychologic anomalies has been admitted they were always regarded as secondary and never as primary in nature. Prejudice against psychiatry is still very common. As a result of it laboratory findings by those familiar with them are often regarded as more accurate, scientific and respectable, than those of an elaborate psychiatric examination. The highly technical jargon used by both allergists and psychiatrists has often constituted a hindrance to bringing the two approaches closer together. Probably the psychiatrist who is fundamentally interested in communication by words is the greater sinner in this respect. As one who has had a foot in the camp of both the allergist and the psychiatrist, the present writer will try to present the psychiatrists' viewpoint on allergic diseases in plain English.

EVIDENCE IN SUPPORT OF PSYCHOLOGICAL FACTORS IN ALLERGIC DISEASES

Evidence in support of the assumption that psychological factors play a part relevant to the etiology of allergic disorders can be summed up under the following headings: (1) the inadequacy of immunobiologic findings in some patients suffering from allergic disorders, (2) the precipitation of the onset of allergic disorders, of their relapses, and of individual attacks by emotional disturbances, (3) the similarity in personality structure of patients suffering from allergic disorders, (4) the established psychopathology of allergic disorders, (5) the interchangeability of allergic disorders with gross psychiatric disorders, and (6) the responsiveness of allergic disorders to psychotherapy.

These items will be successively dealt with. Bronchial asthma, urticaria, eczema, and hay fever will be used as illustrative examples. A discussion of the relationships between psyche and allergy will round off this paper.

The Inadequacy of Immunobiologic Findings in Some Patients Suffering From Allergic Disorders.—Nobody will deny that, in hypersensitive individuals, contact with sufficient pollen will give a response typical of the mode of administration. Neither will it be denied that in a significantly large number of patients suffering from asthma or allied disorders, an offending allergen cannot be traced by the usual diagnostic procedures and that a positive skin reaction is not an infallible criterion of the pathogenic effect of the suspected substance.

From the Allan Memorial Institute of Psychiatry, McGill University, Montreal, Canada.
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Mitchell, Curran, and Myers,[22] for example, compared 200 allergic patients with a vasomotor group of 400 patients. All the patients in the allergic group, which consisted of people suffering from ragweed hay fever and from extrinsic perennial asthma, showed positive skin tests (by the prick method) to substances which correlated with the clinical history. In three quarters of the cases of the vasomotor group classified as perennial vasomotor rhinitis, intrinsic asthma, and chronic urticaria, the skin tests were negative, and the clinical histories and clinical trial failed to afford any positive evidence that specific antigens could be causing the symptoms. Therapeutic results by allergic as well as other methods were uncertain, unpredictable, and generally unsatisfactory. The remainder of the vasomotor group consisted of 100 patients manifesting atopic eczema. In more than half of these 600 patients studied, no specific allergy could be established by skin tests, clinical histories, or clinical trial.

The conclusion to be drawn from these and similar observations is that in a high proportion of patients suffering from disorders labelled allergic, no evidence of allergy can be found, and that either present procedures of examination are inadequate or factors other than allergy play an etiologic part. It must be admitted that the psychologic factor may be one of them.

The Precipitation of the Onset of Allergic Disorders, of Their Relapses, and of Individual Attacks by Emotional Disturbances.—

Bronchial Asthma.—The view that asthmatic attacks can be brought on by emotional disturbances can be traced back to Hippocrates[34] who recognized that anger and hostility influence the asthmatic paroxysm.

Interesting is a self-observation of Trousseau[31] who one day believed himself cheated by a servant, a coachman, about the amount of oats used. Excited, he ordered the oats to be measured. On this occasion he had an attack of asthma. Then he continues: "A hundred times on the streets of Paris or on our boulevards, a hundred times on the highways, I have found myself in an atmosphere of oats much thicker than I had then breathed for a very brief moment, and nevertheless I have experienced nothing like it. Due to emotional disturbance produced by the idea of a domestic theft, however unimportant the theft was, my nervous system was upset, and a cause, very small in itself, acted on it with an excessive intensity."

A patient of Bergson[3] had an attack shortly after being awakened by a fire alarm; one patient of Marx,[20] after a fright caused by a dog jumping at her and another after swallowing the mercury of a broken thermometer; one of our patients when a chandelier fell from the ceiling right in front of him.

In addition it has been shown that emotional disturbances frequently precede the onset of bronchial asthma. Typical of many others is the case of a 26-year-old woman, who had suffered from asthma since her tenth year. At that time her mother had smallpox, and, because of a lung complication, was "gasping for breath like an asthmatic." As it was believed that the mother would die, the children were taken to her sickbed. The impression of the sight of her mother fighting for breath was exceedingly strong. A few days later the patient's asthma commenced and continued even when the mother recovered.[34]

According to Halliday,[10] all of 30 consecutive asthmatics who came under his observation either showed evidence of severe psychoneurotic difficulties in the period preceding the first attack of asthma, or the onset of the asthma followed closely upon some significant emotionally disturbing event. In 37 out of 50 consecutive cases an emotional component in their asthmatic attacks was recorded by McDermott and Cobb.[21]

Urticaria.—A patient of Kreibich and Sobotka[14] usually had attacks of urticaria after annoyance. The correlation was tested by experiment in which the patient was wrongly accused of some little irregularity on two occasions by the nurse. The patient became annoyed and within a few minutes an urticarial rash broke out. A similar experiment was performed by Dufke[5] on a woman who developed urticaria whenever she came in contact with silk. When linen was applied nothing happened until she was told that the linen was silk, whereupon the eruption developed. An unplanned experiment was described by Hansen[11] in which a woman who was dining with a male friend at a rendezvous was surprised by her husband appearing on the scene. The results were terror and generalized urticaria. This situation involved a conditioning for the patient who was eating lobster when surprised. She always suffered from urticaria after eating lobster subsequently, though never before.

Stokes, Kulchar, and Pillsbury[30] detected relevant psychogenous stress in 83 per cent of 100 patients studied for urticaria.

Eczema.—Two examples may suffice to demonstrate the precipitating effect of emotional disturbances in eczema. An officer had spent the night drinking heavily. The morning after, he vaguely remembered that he had had sexual intimacy with a lady of easy virtue while he was drunk. He had been happily married for 17 years and had never before been unfaithful to his wife. After the incident he was full of remorse. A few days later he developed an eczema on the manipulating finger. Another patient, aged 69, had always thrived on his popularity. After a very hard struggle he had managed to build up a successful business. Gradually, in the years after the 1914 war, the business went down and he had to sell out. After he had paid all his debts he was left with practically nothing. Within a few weeks of this disaster he started to have patches of eczema in the bends of his arms and behind his knees. It cleared up for a few years while he was successfully running an agency for a firm but returned when this firm went bankrupt. The areas affected were his face, his ears and his neck. The irritation was almost unbearable.

In 77 out of 90 patients studied, a correlation between emotional disturbances and eczematous manifestations could be established. Events of a disturbing nature preceded the onset of the eczema in 46 cases.[33]

Hay Fever.—Well known is Morell Mackenzie's[17] case of a "young lady who suffered so acutely from hay fever that she always remained in London until after the hay was got in. On one occasion, however, after a visit to the Royal Academy, where she had been struck with a highly realistic painting of a hayfield . . . she had a severe attack of her familiar complaint." Similarly, a patient of Sir William Osler had an attack of hay fever when given an artificial rose to smell. "This," Sir William Osler says, "strikingly illustrates the neurotic element in the disease."

Freeman[7] relates the following incident: "An imaginative and rather hypochondriacal businessman firmly believed that the yellow mustard flower was the cause of his hay fever symptoms. This is a very easy mistake to make because mustard, like the rose, flowers chiefly in June." Freeman then continues: "I deliberately gave him a word painting of the dusty English lanes in midsummer: the high hedges, the gate on which he could lean gazing at the nearby fields, and the hillside beyond them in the afternoon sunlight ablaze with the yellow mustard. At this point the patient interjected. 'Stop, stop, you are giving it to me' and I found his eyes were red and streaming."

Abramson[1] treated a theological student who stated: "When I have hay fever during September, something quite interesting occurs. I may have hay fever prior to the preaching, but the hay fever disappears when I reach the pulpit."

The Similarity in Personality Structure of Patients Suffering From Allergic Disorders.—These observations show no more and no less than that emotional factors, in certain cases, precipitate allergic manifestations. They do *not*, however, show that emotional factors are responsible for the etiology of allergic disorders. To prove this it would be necessary to demonstrate that patients suffering from allergic disorders are similar in personality structure and that manifestations usually labelled allergic are either concomitants of primitive biological urges or symbolic representations of primitive emotional conflicts.

Bronchial Asthma.—Consensus of opinion exists that, however much their superficial behaviour may vary, asthmatics have in common a deep-seated emotional insecurity and an intense need for parental love and protection. Fear of losing their mothers' support, good will, and love is an outstanding feature of their premorbid personalities. Their sense of insecurity may be overtly displayed or it may be overlaid and masked by defense reactions of which overhelpfulness, denial, and confession are the most important ones.

Situations which provoke asthmatic attacks are almost invariably of such a nature as to rouse fear of losing the love of the mother or of a mother substitute. This fear may be roused by impending separation from the mother, by the birth of younger children, or by sibling jealousies (French and Alexander).[8]

Urticaria.—Two-thirds of 35 urticaria patients studied stated spontaneously that they missed parental and especially maternal affection as children. Their belief that they were unloved, or unfairly treated appeared to be justified in some instances. Yet more often than not, it was ill founded or entirely unfounded.

In about equal numbers these patients reacted to a situation which was in fact, or at least for them, frustrating in an aggressive or in a submissive way. In other words, they either openly expressed their resentment without realizing why they were doing it, or they suppressed, or repressed, their aggressive response in the hope of having their inordinate needs gratified by their exemplary behaviour.

These two modes of behaviour were maintained in adult life. As adults, roughly half of the patients studied adopted a pleading, overaccommodating and ingratiating attitude toward their environment whereas the other half, far

from begging for what in fact or in fantasy had been denied to them, demanded what they regarded as their due, complained if they did not get what they wanted, became hard and harsh or adopted a manifestly vindictive attitude. The aggressive behaviour of the latter patients arose from various sources: firstly, as has been stated, they were unable to tolerate any denial of love and reacted violently to any real or imagined situation of this kind—aggressive response; secondly, they were unable to admit their inordinate need for affection and therefore hid it behind a brusque, aggressive, and often irritating façade—aggressive defence; thirdly, it appears that at least some of these patients compulsively repeated the childhood trick of "working up for a slap"; just as then they tried out how far they could go without being punished—perhaps in the vain hope that other people would like and love them despite their objectionable behaviour.

Disturbing events entailing anticipation or actual withdrawal of love frequently preceded the onset of urticaria and of its relapses. They include such events as desertion or impending desertion by husband, wife, or sweetheart, real or imagined lack of love in marriage, and departure of the husband for service abroad.[36]

Eczema.—Irrespective of how many and which other factors are of relevance to its etiology, atopic eczema is a disease which occurs in emotionally insecure individuals. A majority of the 90 patients studied felt that they had not had their fair share of affection as children, and were apt to carry over into adult life an undue, childlike dependence on either of their parents or both—usually the mother. Their need for affection, attention, support, and protection may find overt expression in the form of submissiveness, docility, or display of helplessness. Or, by way of overcompensation, their need may be concealed behind ambition, self-drive, self-assertive or provocative behaviour. Frequently lack of self-confidence proved a serious handicap in their social relationships and occupational achievements. A fair number of our patients were afraid of carrying the responsibilities of married life. If they did marry, their partners often ostensibly served as parent substitutes. Typically one patient, a businessman aged 45, could only resist the urge to scratch himself if his wife, a very motherly type of woman, sat by his bedside and held his hand. She described him as their third child.

Any situation which endangers or shatters the delicately balanced sense of security of these individuals may precipitate the onset of eczema or of relapses—in particular the loss of a key figure from the patient's environment. Thus one of our patients developed eczema after his wife had run off with another man, another after he had gone bankrupt and a third when, after her long postponed marriage, she was torn in her loyalties toward her husband and her mother with whom she shared a flat.

Hay Fever.—Finally, the test case for the validity of the theory that persons suffering from allergic diseases have certain features in common is, of course, that of hay fever, the classical allergic disease. Very few hay fever patients have been subjected to psychoanalysis. In three analysed patients, Leon Saul[29] found deprivation of maternal love in childhood with consequent strong passive

attachment to the mother or a mother substitute as a central feature. Attacks occurred regularly when the patients were in situations in which demands were made on them which they felt obliged to meet but from which they wished to escape to their mother.

The Established Psychopathology of Allergic Disorders.—It has been shown that emotional factors frequently precipitate the onset and individual attacks of allergic disorders and that according to the observations of various independent observers, patients suffering from different allergic disorders have certain personality features in common. The most outstanding feature is a strong longing for love, a longing of the infantile dependent kind, of the child for his mother. It arises from a sense of deprivation of maternal love in childhood and leads to a passive dependent relationship to the mother and to a fear of estrangement from the mother and of being left alone. Situations which rouse and reactivate these fears precipitate the onset of allergic disorders, of relapses, and of individual attacks.

Patients suffering from allergic diseases protect themselves against their basic sense of insecurity by means of various defence mechanisms of which overhelpfulness, denial and confession have been mentioned. Moreover, a substantial number of allergic patients, unrecognized by themselves, endeavor to obtain emotional security by virtue of their exemplary behaviour. It seems that the belief[2] that allergic patients are superior in intelligence has come about because of their tendency to buy love by good performance.

It may be objected that there are, of course, many persons who have conflicts and personalities similar to those described but who do not suffer from allergic diseases. *To account for the somatic manifestations of allergic patients one must assume that they are constitutionally predisposed to the disorders which they develop and that specific psychodynamics are operative in them which do not exist in those who despite a similar conflict constellation enjoy perfect health or suffer from different psychosomatic afflictions.*

Why do individuals who express longing of an infantile kind for maternal love in the form of psychosomatic disease develop different psychosomatic diseases? In answering this question the following factors must be borne in mind: an infant's longing for the mother may be directed toward sucking or eating, or toward protection, shelter, bodily contact, warmth and caressing. His means of attracting her attention may be inarticulate sounds, crying and afterward talking, he may stretch out his arms pleadingly or if his request is not fulfilled he may scream with fury at the top of his voice.

It has been suggested that the choice of symptom in psychosomatic disease is determined by an unconscious infantile desire, by the means of expressing and obtaining gratification of this desire and by the response to frustration. Persons who, on the infantile model, substitute need for food for need for affection are apt to develop psychosomatic gastrointestinal disorders or they may become obese through overeating, while persons whose infantile need is for protection, shelter, bodily contact, warmth, and caressing are apt to develop psychosomatic skin diseases. The asthmatic calls out for help in a disguised manner, the eczematous patient stretches out his arms and expresses his need

by this gesture, whereas the urticaria patient by his urticarial swellings demonstrates a token of the skin manifestations of infantile fury. It has been said that the manifestation of all three disorders—asthma, eczema, and urticaria—are equivalent to crying. The asthmatic suppresses the cry, the eczematous patient cries *through* the skin and the urticaria patient cries *into* the skin.

This theory is not quite so fantastic as it sounds because it has been supported by clinical and experimental evidence.

Saul and Bernstein[28] report the case of a girl who was greatly distressed by the birth of an illegitimate child. Since the birth of this child three months before she had cried almost continually. One evening she was told that if she wept so much she might be found committable. She stopped crying and in the morning she had a generalized urticaria, chiefly of the chest, back and arms. After several days she was told that a good cry would make her feel better. The following morning the rash was gone.

In an experimental investigation of skin exudation, Kepecs, Robin and Brunner[12] produced cantharides blisters in patients suffering from atopic dermatitis, exfoliative erythroderma and urticaria and in subjects with nonpathologic skins. The tops of the blisters were cut off leaving freely oozing surfaces. There was a sharp rise in the fluid level associated with weeping both in patients with skin diseases and in controls. Inhibition of weeping resulted first in a drop in exudation rate, followed by a rise indicating a tendency to break through the inhibition at the blister site.

Interchangeability of Allergic Disorders With Gross Psychiatric Disorders.—The low incidence of asthma in mental institutions has been known for a long time. MacInnis[16] surveyed two hospitals with a total patient population of over seven thousand. During a five-year period there were only 5 cases of asthma. Leavitt[15] in a survey of 11,647 patients with a "functional" psychosis found only 10 cases of asthma, i.e., an incidence of 0.08 per cent. It appears doubtful whether this low incidence can be attributed solely to an environment relatively free of extrinsic allergens. A number of cases have been reported in which a mental illness substituted for asthma: one by Oberndorf[25] in which manic attacks substituted for the asthma; another by Saul[29] in which the asthma alternated with either a manic or a depressive phase of a manic-depressive psychosis. Kesselbaum[13] studied 10 cases of dementia precox, and Myerson[24] and Malamud[18] each had one case in which the asthmatic attacks ceased with the onset of the mental illness.

Gillespie,[9] Ziegler and Elliott,[37] and the present writer have each reported a case of a patient who developed anxiety attacks during asthma-free periods. My patient came to our asthma department not because he suffered from asthma but because he wanted to have it back. He had lost his asthma after Coué treatment somewhere else but preferred it to the severe anxiety attacks which had taken its place.[34]

The Responsiveness of Allergic Disorders to Psychotherapy.—An assessment of the value of psychotherapy in the treatment of allergic disorders is difficult for a variety of reasons: (1) no large numbers of patients treated by the same psychiatrist are available because of its time-consuming nature; (2) psychiatrists

are apt to publish successes rather than failures; (3) patients referred to psychiatrists are of necessity selected either on the grounds that they are refractory to any other form of treatment or that they display gross psychiatric anomalies; and (4) superficial forms of psychotherapy such as hypnosis, are likely to give less favourable and less permanent results than those which assail the total personality, such as psychoanalysis. Bearing all this in mind, the results of psychotherapy are by no means unsatisfactory.

A survey[27] published in 1929 covers psychotherapeutic results obtained in 43 asthmatics treated by 18 different authors; methods of psychotherapy employed ranged from waking suggestion and sedative hypnosis to psychoanalysis. Two of these 43 patients were treated unsuccessfully, three were reported as improved, fifteen had relapses after previously successful treatment and twenty-three, i.e., approximately half of the patients treated, were described as "cured." The best results were obtained from those methods which have as point of attack the total personality. Wilson[32] reports on therapeutic results obtained in nineteen asthmatics who were under psychoanalytic treatment six months or more. Nine were symptom-free, 8 were much improved, and 2 were unchanged, at the time of the report. The follow-up of some of these cases extends over more than 35 months.

A follow-up of 21 patients suffering from atopic eczema recently treated along analytical lines showed that seven were greatly improved and seven had lost their eczema completely.[33]

Consensus of opinion is that psychotherapy does not alter the fundamental allergic background but that it allows the allergic individual to come into contact with the noxious allergen with impunity. Numerous examples to this effect have been reported. For instance, in three cases of typical horse allergy with proved highly positive cutaneous test, Hansen[11] succeeded in giving relief from attacks by hypnotic treatment.

INTERRELATIONSHIPS BETWEEN PSYCHE AND ALLERGY

Experiments.—(1) A demonstrable cutaneous allergy cannot be produced by suggestion. A patient especially suitable for these purposes was, under hypnosis, given the suggestion that the scent of roses was harmful to her. It was easy to produce in this asthmatic patient the conditioned reflex so that, even in a waking state, the slightest smell of roses, and even the belief that roses were in the vicinity, was sufficient to produce asthmatic attacks. However, a cutaneous test with rose extract, performed after several weeks of training, was negative.[34] (2) A demonstrable cutaneous allergy can be impaired by suggestion. Diehl and Heinichen[4] succeeded in influencing the extent of the allergic skin reaction by suggestion under hypnosis. They suggested to their experimental subjects—two asthmatic persons and a healthy but skin sensitive person—a diminution of irritation of the forming wheal and a reduction in its development. Without suggestion the size of the wheal on repetition fluctuated 15 per cent under carefully controlled conditions; after suggestion a reduction in the size of the wheal of over 40 per cent was observed. Their ability to change a wheal reaction to an allergen has been confirmed by the observations

of Marcus and Sahlgren,[19] who, in a female psychopath, succeeded in demonstrating that her cutaneous reactivity to linoleum extract to which she was sensitive, could be inhibited almost completely by suggesting under hypnosis that the injected allergen was another substance. The same inhibitions were obtained in a case of pollen extract, and it was even found possible to inhibit a tuberculin reaction. (3) With a cutaneous allergy existing unabated, the asthma-producing effect of the allergen can be inhibited by suggestion. A tobacco saleswoman, hypersensitive to tobacco, regularly had asthma attacks after contact with tobacco. These attacks also occurred when the patient was not aware of contact with the allergen (e.g. after subcutaneous injection of tobacco extract). By hypnotic order the occurrence of attacks after inhalation or subcutaneous injection of the noxious allergen could be inhibited. Skin reactivity to tobacco remained positive.[34]

Clinical Observations.—Clinically patients suffering from allergic disorders can be divided into three groups: (1) In a considerable number of patients the clinical manifestations are no doubt sufficiently accounted for by an inborn or acquired allergy, i.e., on an entirely organic basis. (2) There is a group of patients labelled allergic in whom no offending allergen can be traced by the usual diagnostic procedures. Positive psychiatric evidence in these cases indicates that in them emotional states of the nature described lead to physiological changes which imitate and are to all appearances identical with those observed in allergic diseases proper. The term para-asthma has been suggested by Peshkin[26] for this group. (3) There are patients in whom evidence of both a specific hypersensitivity and specific emotional states exist and in whom owing to a clear correlation between emotional disturbances and clinical manifestations it must be assumed that the emotional disturbances act as a catalyst on a dormant allergic predisposition.

Errors.—Regrettable errors have occurred owing to neglect of the psychiatric aspects by allergists and of the allergic aspects by psychiatrists. For instance, the case of an actress has been reported who always had an asthma attack before her appearance on stage. Stage fright was supposed to be responsible until it was found that an ingredient of her make-up caused the asthma.[6] Conversely, a patient of Moos[23] regularly had attacks of asthma in the evening when supper was being prepared. The kitchen-smell was believed to be the cause of the asthma, and all doors were kept carefully closed. It was, however, revealed that a conversation at supper which had extremely excited the patient caused the time-fixation.

Treatment.—Hence neither the allergic nor the psychiatric aspects of the disease should be neglected in treatment. The physician should treat the patient and not his allergy alone. On examination an assessment of the relative degree and relative significance of allergic and emotional factors should be made and the patient should be treated accordingly.

In some patients emotional factors are of minor importance, in others they deserve serious consideration, in still others they are all-important.

It may be debatable whether psychotherapy should be combined with desensitization and symptomatic forms of treatment. From a scientific point of view such a combination may be objectionable; from the practical point of view palliative treatment is often unavoidable.

In many patients it may be sufficient to allow the patient to unburden himself. Physicians may be surprised how easily patients talk once an opportunity to do so has been given to them. The physician should be a benevolent listener and should under no circumstances adopt a moralistic attitude. Advice is usually contraindicated; the patient should be left to make his own decisions. More often than not, emotional conflicts do not lend themselves to a solution by change of environment. Generally speaking, it is in the interest of the patients that the physician—and the physician alone—deals with both their allergy and their emotional problems; in a limited number of patients only is the service of a psychiatrist required. His functions consist of making a psychosomatic assessment, and, if deemed necessary, giving systematic psychotherapy.

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American Academy of Allergy

EIGHTH ANNUAL MEETING, HOTEL SHERMAN, CHICAGO, ILL.,
FEB. 18, 19, AND 20, 1952

Program

Monday, February 18, 1952
Morning Session, 9:15 A.M.
Ben Z. Rappaport, Chicago, Presiding

Molds in House Dust and Furniture Stuffing. Mary Ann Swaebly and Clyde M. Christensen, Ph.D., University of Minnesota.

The Relation of Route of Injection of Antigen to Antibody Production. Milton M. Mosko, M.D., Elmer L. Becker, Ph.D., M.D., and J. Munoz, M.D., Chicago, Ill.

Studies in Atopic Dermatitis. IV—Importance of Pollen (Especially Ragweed) as Inhalant Factor. Louis Tuft, M.D., and V. Muriel Heck, M.T., Philadelphia, Pa.

Intermission

Graduate Training and the Specialties. Edward H. Leveroos, M.D., Chicago, Ill., Associate Secretary, Council on Medical Education and Hospitals, American Medical Association.

Asthma Deaths: A Study of 130 Necropsy Records and 100 Clinical Records of Patients Who Did Not Come to Autopsy. Stearns S. Bullen, M.D., Rochester, N. Y.

Allergy Problems as Seen in Twins. Ralph Bowen, M.D., Houston, Texas.

Increase in Castor Bean Allergy Due to Fertilizer. Willard S. Small, M.D., Pasadena, Calif.

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Monday, February 18, 1952
Afternoon Session, 2:00 P.M.
Walter S. Burrage, Boston, Presiding

The Use of Tissue Cultures in the Study of Allergic Reactions. Charles M. Pomerat, Ph.D., Professor of Cytology, Texas University School of Medicine, Galveston, Texas.

Intermission

Neutralizing Antibody in Non-Allergic Individuals. Saul Malkiel, M.D., and Samuel M. Feinberg, M.D., Chicago, Ill.

Immuno-Serological Studies of the Immediate Wheal-Type Allergies. Arthur E. O. Menzel, Ph.D., Walter R. Kessler, Ph.D., M.D., Robert A. Cooke, M.D., and Phyllis A. Myers, B.A., New York, N. Y.

Disability Due to Inhalation of Grain Dust. Victor L. Cohen, M.D., and Howard Osgood, M.D., Buffalo, N. Y.

Migraine Is an Allergic Disease. Albert H. Unger, M.D., Chicago, Ill.

Is Migraine an Allergic Disease? Michael Schwartz, M.D., Copenhagen, Denmark.

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Tuesday, February 19, 1952
Morning Session, 9:00 A.M.
Theodore L. Squier, Milwaukee, Presiding

Anaphylaxis in the Pertussis Immune-Histamine Sensitive Mouse. Saul Malkiel, M.D., and Betty J. Hargis, B.S., Chicago, Ill.

Pharmacologic and Anaphylactogenic Properties of Staphylococcus Protein and Unfractionated Extract. Murray Dworetzky, M.D., Benjamin R. Zeitlin, M.S., Morton C. Kahn, D.Sc., and Horace S. Baldwin, M. D., New York, N. Y.

A Suggested Method for Quantitative Evaluation of Ragweed Sensitive Hay Fever and Asthma Patients. Robert A. Stier, M.D., Wm. C. Grater, M.D., and Samuel M. Feinberg, M.D., Chicago, Ill.

Gastric Lesion of Loeffler's Syndrome. J. P. Ruzic, M.D., J. H. Dorsey, M.D., H. L. Huber, M.D., and J. H. Armstrong, M.D., Chicago, Ill.

Intermission

Effect of Cortisone Upon the Rise of Serum Antibody Level After the Injection of a Saturating Dose of Antigen in Rabbits. Bernard N. Halpern, M.D., G. Maurice, M.D., A. Holtzer, M.D., M. Briot, and Pasteur Vallery-Radot, M.D., Paris, France.

The Induction of Asthmatic Attacks in a Closed System With Spirometric Studies. Francis C. Lowell, M.D., Irving W. Schiller, M.D., and Alice Lowell, Boston, Mass.

The Induction of Asthmatic Attacks With Aerosolized Extracts of House Dust. A Clinical Study. Irving W. Schiller, M.D., and Francis C. Lowell, M.D., Boston, Mass.

Histaminase Activity of Plasma in Allergic Patients During Pregnancy. Bram Rose, M.D., and E. V. Harkness, M.D., Montreal, Canada.

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Tuesday, Feb. 19, 1952

Afternoon Session, 2:00 P.M.

Stanley F. Hampton, St. Louis, Presiding

Contributions of Immunochemistry to the Study of Allergic Reactions. Elvin A. Kabat, Ph.D., Associate Professor of Bacteriology, College of Physicians and Surgeons, New York City.

Intermission

The Effect of Pyribenzamine on Passively Sensitized Sites. Bernard B. Siegel, M.D., Katherine L. Bowman, A.B., and Matthew Walzer, M.D., Brooklyn, N. Y.

The Use of Antigen-Coated Particles for the Detection of Antigen-Antibody Reactions as Applied to Hypersensitive Sera. Delna W. Garrison and John M. Sheldon, M.D., Ann Arbor, Mich.

Differential Cell Counts in the Blister Fluid of Allergic Eczematous and Irritant Bullous Lesions. Rudolph Baer, M.D., New York, N. Y., and Meyer Yankowitz, M.D., Miami, Fla.

President's Address

Horace S. Baldwin, M.D.

Annual Business Meeting, 4:30 P.M.

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Wednesday, Feb. 20, 1952
Morning Session, 9:00 A.M.

Panel Discussion on ACTH and Cortisone and Their Use in the Allergic Diseases.

Moderator, William B. Sherman, New York. Panel: Carl E. Arbesman, M.D., Buffalo; Walter S. Burrage, M.D., Boston; Samuel M. Feinberg, M.D., Chicago; Leslie N. Gay, M.D., Baltimore; Jerome Glaser, M.D., Rochester, New York; Stanley F. Hampton, M.D., St. Louis; Francis C. Lowell, M.D., Boston; and Ben Z. Rappaport, M.D., Chicago.

The discussion will be divided into two parts providing for an intermission at approximately 10:30 A.M. Questions and discussion from the floor are urged. It will facilitate the discussion if questions are submitted to the moderator in writing.

The Panel Discussion will be based on the following papers:

Intravenous ACTH for Bronchial Asthma. Carl E. Arbesman, M.D., Max Schneider, M.D., David Greene, M.D., and Howard Osgood, M.D., Buffalo, N. Y.

Maintenance Cortisone in Bronchial Asthma. Walter S. Burrage, M.D., and John W. Irwin, M.D., Boston, Mass.

An Objective Assay of Ragweed Hay Fever and Asthma Treated With Cortisone Out-of-Season and In-Season. Robert A. Stier, M.D., Samuel M. Feinberg, M.D., Saul Malkiel, M.D., and Margaret Werle, Chicago, Ill.

A Clinical Report on the Treatment of Contact Dermatitis With Adrenecorticotropic Hormone in Oil. Leslie N. Gay, M.D., and George W. Murgatroyd, Jr., M.D., Baltimore, Md.

The Treatment of Atopic Dermatitis in Infants and Children With ACTH and Cortisone. Jerome Glaser, M.D., Rochester, N. Y.

Intravenous ACTH in the Treatment of Allergic Diseases. Stanley F. Hampton, M.D., St. Louis, Mo.

Prolonged Treatment of Bronchial Asthma With Cortisone and ACTH. Francis C. Lowell, M.D., Irving W. Schiller, M.D., Wm. Franklin, M.D., and Samuel Leard, M.D., Boston, Mass.

Histochemical Studies on the Effect of ACTH on the Nasal Mucosa of Patients With Ragweed Pollinosis. Ben Z. Rappaport, M.D., Max Samter, M.D., H. R. Catchpole, Ph.D., F. Schiller, M.D., and C. Bader, B.A., Chicago, Ill.

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To Be Read by Title

Intrinsic Asthma Francis M. Rackemann, M.D., Boston, Mass.

Epinephrine Base Suspended in Water With Thioglycollate. Hyman Naterman, M.D., Boston, Mass.

Indications and Contraindications, Avoidable and Unavoidable Complications, in ACTH and Cortisone Therapy in Bronchial Asthma. Alvan L. Barach, M.D., New York, N. Y.

Allergic Factors in the Pathogenesis of Bronchiectasis. Oscar Feinsilver, M.D., Worcester, Mass.

Congenital Laryngeal, A Prelude to Allergy. Abraham B. Schwartz, M.D., Milwaukee, Wis.

Contribution to the Study of the Reticulo-Endothelial Origin of Dust Cells or Alveolar Macrophagi. E. A. Pedace, M.D., A. E. Bachmann, M.D., and G. Ruiz Moreno, M.D., Buenos Aires, Argentina.

The Asthmatic Patient as a Problem of the Hospital Emergency Room: A Survey. George Watson, M.D., and Leslie N. Gay, M.D., Baltimore, Md.

Asthma in the Preschool Child. Claude A. Frazier, M.D., and Robert A. Cooke, M.D., New York, N. Y.

Placental Transfers of Antibodies. Claude A. Frazier, M.D., and William Sherman, M.D., New York, N. Y.

Quantitative Studies in Skin Testing. Henry H. Swain, M.S., M.D., and Elmer L. Becker, Ph.D., M.D., Chicago, Ill.

17-Ketosteroid Determination—A Modified Method Which Corrects for the Interference Due to Adrenocorticosteroids. Marguerite Lambert, and John M. Sheldon, M.D., Ann Arbor, Mich.

Evaluation of Patterns in Contact Dermatitis of the Hands. G. L. Waldbott, M.D., Detroit, Mich.

Report on the Use of Group Psychotherapy in Neurodermite (Atopic Eczema). Hyman Miller, M.D., Beverly Hills, Calif.

The Role of Adrenals in Allergy—A Critical Review. Leo Criep, M.D., Pittsburgh, Pa.

Ragweed Invasion of Oregon. Frank Perlman, M.D., Portland, Ore.

Studies on Hydrolyzed Oral Pollen, Suggestions for Procedures for Further Study on Oral Pollen Antigens. Earl B. Brown, M.D., and Walter Kessler, M.D., New York, N. Y.

Asthma in Patients Over the Age of Fifty Years. John L. Guerrant, M.D., Charlottesville, N. C.

Classification of Asthma. Oscar Swineford, Jr., M.D., John L. Guerrant, M.D., and Alexander McCausland, M.D., Roanoke, Va.

Depot Therapy With Water-in-Oil Emulsions of Pollen Extract. Mary H. Loveless, M.D., New York, N. Y.

Effect of Cortisone on the Bacterially Sensitized White Cell. Hermann Blatt, M.D., Cincinnati, Ohio.

The Pathological Changes in the Brain Produced by Reversed Anaphylaxis in the Guinea Pig and the Effect of ACTH and Cortisone Thereon. Kornel Terplan, M.D., Carl E. Arbesman, M.D., Erwin Neter, M.D., and Les Bertram, M.D., Buffalo, N. Y.

Postgraduate Course in Allergy

February 15, 16, and 17, 1952
Chicago, Illinois

TECHNIQUES OF EXPERIMENTAL IMMUNOLOGY
AS APPLIED TO ALLERGY

Hotel Sherman
Friday, Feb. 15, 1952
1:00 P.M.—6:00 P.M.
7:30 P.M.—9:00 P.M.

A symposium of immunologists and immunochemists which will outline in simple terms physical, chemical and immunological methods and their application in the study of allergy.

TOPICS

Physical Methods: Electrophoresis and Ultracentrifuge
Quantitative Precipitin Techniques
Complement Fixation Tests
Schultz-Dale Technique
Tracer Techniques

FACULTY

DR. PAUL R. CANNON, *Professor of Pathology*, University of Chicago, Introduction
DR. ELMER L. BECKER, *Ass't Professor of Bacteriology*, University of Illinois
DR. SAMUEL BUKANTZ, *Ass't Professor of Medicine*, Washington University
DR. E. JACK COULSON, *Biochemist*, Allergen Research Division, United States Department of Agriculture
DR. FRANK DIXON, *Professor of Pathology*, University of Pittsburgh
DR. SAUL MALKIEL, *Ass't Professor of Medicine*, Northwestern University

Roundtable Discussion From 9:00 to 10:00 P.M.

A VISITING ALLERGY CLINIC
A Postgraduate Course in Action
Hotel Sherman
Saturday, Feb. 16, 1952

The Visiting Allergy Clinic represents a new venture of the Subcommittee on Postgraduate Education—an attempt to combine didactic and "bedside" teaching. Residents and attending staff of universities and hospitals in Chicago will present patients to guest lectures for diagnostic and therapeutic comment and advice.

9:00 A.M. to 12:00 Noon
Bronchial Asthma and Emphysema
1:00 P.M. to 4:30 P.M.
Complications in Allergic Diseases
Uncommon Allergic Disorders

FACULTY

DR. HARRY L. ALEXANDER
DR. J. HARVEY BLACK
DR. ROBERT A. COOKE
DR. HYMAN MILLER
DR. GEORGE PINESS
DR. FRANCIS M. RACKEMANN
DR. BRET RATNER
DR. WILL C. SPAIN
DR. OSCAR SWINEFORD, JR.
DR. LOUIS TUFT
DR. WALTER L. WINKENWERDER

A COURSE IN DERMATOLOGIC ALLERGY

Hotel Sherman
Sunday, Feb. 17, 1952
9:00 A.M. to 4:30 P.M.

The aims of the Course are primarily practical. The emphasis will be on morphologic recognition and the differential diagnosis of various allergic dermatological entities, inasmuch as it is felt that it is this aspect of allergic dermatoses in which the allergist is principally weak. While the emphasis will be on the aforementioned, all other important aspects will be taken up; namely, the methods and techniques of determining the causal substance for a given allergic dermatosis, therapy, both topical and systemic, and psychosomatic aspects. Finally, there will be introductory comments on the theory classification and pathology of allergic dermatoses.

TOPICS

Definition of Allergy
Classification of Allergic Sensitizations
Classification of Allergic Dermatoses
Pathology of Allergic Dermatoses and of Allergic Reactions
The Investigation of Chronic Urticaria
Drug Reactions
Psychosomatic Aspects of Allergic Dermatitis
The Nonimmunologic Therapy of the Common Allergic Dermatoses
Id Reactions
Infantile Eczema and Atopic Dermatitis
Eczematous Contact Eruptions

FACULTY

DR. LOUIS A. BRUNSTING, *Professor of Dermatology and Syphilology,* Mayo Foundation, Rochester, Minnesota
DR. STEPHEN EPSTEIN, *Clinical Associate Professor of Dermatology,* University of Minnesota.
DR. FRANCIS W. LYNCH, *Clinical Professor,* Division of Dermatology, University of Minnesota
DR. ADOLPH ROSTENBERG, JR., *Professor of Dermatology,* Associate Director of the Allergy Unit, University of Illinois
DR. STEPHEN ROTHMAN, *Professor of Dermatology,* University of Chicago
DR. OSCAR SWINEFORD, JR., *Professor of Internal Medicine,* University of Virginia
DR. JAMES R. WEBSTER, *Professor of Dermatology,* Northwestern University

IDENTIFICATION AND BIOLOGY OF FUNGI AND POLLEN

Feb. 15, 16, and 17, 1952
Northwestern University Medical School
Chicago Campus

An intensive and practical course in identification and biology of fungi and pollen, and survey techniques. The Course will be given under the auspices of the Council on Aeroallergens of the Research Council of the American Academy of Allergy.

FACULTY

Professor CLYDE CHRISTENSEN, University of Minnesota
DR. OREN C. DURHAM
DR. RALPH F. VOIGT, University of Illinois
DR. SIDNEY FRIEDLAENDER

The Course Is Open to Physicians and Technicians

The Subcommittee on Postgraduate Education gratefully acknowledges a grant from Baxter Laboratories of Morton Grove, Illinois, which has been made in support of this Course.

Preliminary Report of the Pollen Survey and Herbarium Committees for the 1951 Season

At the time of preparation of this report in late November, pollen counting is still in progress in some of the southern cities and not all reports are in from other parts of the country. Interest in pollen surveys is spreading rapidly to more distant parts of North America and even to Europe and Asia. A dozen local studies, complete for all pollens from spring to fall, have been made in Alberta; original surveys have been made in three Canadian national parks, including Banff and Lake Louise; and fifteen new local ragweed surveys are reported from the Maritime Provinces. One atmospheric test series was carried out in the Virgin Islands, and field checks were made during the late fall in Puerto Rico, Hispanola, Jamaica and Cuba. Florida has seven new stations this year in addition to most of the fifteen where studies were instituted last year by the Florida State Department of Health. The Detroit City Health Department has carried on an intensive city-wide ragweed study involving simultaneous air tests in twenty-three locations. New collaborators are reporting from at least five other states. Of special interest is the work being done in the Wenatchee Valley, Washington, where short ragweed has spread rapidly in the orchards in recent years. Strangely enough, at Medicine Hat in southeastern Alberta, ragweed has gained its only known foothold in western Canada (Index 11). The other ten stations in Alberta showed only traces of ragweed pollen on the slides or none at all. In Florida only Tampa seems to be making a bad record this year, but the season is not done.

Since last year's ragweed pollen concentrations in the populous Great Lakes area were unusually light, due to generally cool, unfavorable weather, it was only to be expected that most cities of that section would show a decided increase this year over 1950. Almost without exception this was the case in eastern Iowa, Wisconsin, Illinois, Indiana, Michigan, Ohio and western New York. Here the apex of ragweed concentration occurred in almost every city within two days of the end of August. By some freak of weather in eastern Ohio and western Pennsylvania the climax for this local area was delayed until the 21st of September. In the seaboard area from Boston to Norfolk the ragweed catch averaged a little heavier than last year—some places less, some more—with apexes scattered from the 30th of August until the 11th of September. This variation in the climax date was specially apparent in the Greater New York and Long Island Sound region, indicating a lack of strong wind movement at any time during the period of heavy ragweed pollination.

Accessions to the Herbarium this year have not been numerous, but a few reliable collectors have added some very valuable pollens. A generous assortment of authentic specimens was furnished to each student attending the short course in aerobiology given by the Pollen and Mold Committees at Cornell University in February. A steady demand for pollens has been experienced through the year, but many allergists are still unaware of the excellent free service available to them.

Oren C. Durham, Chairman
Pollen Survey Committee and
Herbarium Committee

Announcements

Allergy Meeting in Melbourne, Australia, August, 1952

Dr. Charles Sutherland, Fellow of the Academy and Chairman of the Section on Allergy of the Australasian Medical Congress, has informed the Academy's International Committee that this Congress will be held in Melbourne in August, 1952, with the Section on Allergy meeting just before or just after the main Congress.

Dr. Sutherland inquires unofficially whether some member of the Academy may not attend the Congress and present a paper before the Section on Allergy. Theirs is a small group with insufficient funds to offer to pay expenses. He suggests that an Academy member might be making a holiday trip in that part of the world, and writes that he would issue an official invitation from the Congress.

Any Academy members who contemplate a trip in that area can notify the International Committee through the Executive Office. This Committee will be notified later of the exact dates of this Congress, and will be glad to assist in making official arrangements with Dr. Sutherland.

Howard Osgood, Chairman,
International Committee.

International Organization for Aerosology

At the recent meeting of the Italian Congress on Aerosol Therapy which was reported in *Science*, Nov. 23, 1951, it was decided to organize an International Organization for Aerosology to include all workers in the field. Any readers who are interested in such an organization, or the formation of an American Society in this field are invited to communicate with Dr. Samuel J. Prigal, 55 Park Avenue, New York 16, N. Y.

Annual Congress of American College of Allergists

The Annual Congress of The American College of Allergists will be held at the Hotel William Penn in Pittsburgh, Pa., April 7-9, 1952. The program will consist of sectional meetings covering Dermatologic Allergy, Otolaryngologic Allergy, Industrial Allergy, Pediatric Allergy and Psychosomatic Allergy, as well as general sessions.

Dr. Alexander Wiener of Brooklyn, New York, will present a guest lecture entitled "The Solution of Certain Fundamental Immunologic Problems by Studies on Rh Sensitization."

The Congress will be preceded by a three (3) day Graduate Instructional Course in Allergy on April 4-6. Details and application blanks for the course may be obtained from Dr. Fred W. Wittich, Sec'y-Treas. American College of Allergists, 401 LaSalle Medical Building, Minneapolis 2, Minn.

Book Reviews

Clinical Allergy. Second Edition by Samuel J. Taub, M.D., New York, 1951, Paul B. Hoeber, Inc., 276 pages, $4.50.

This manual of allergy, first published in 1945, now appears in a second edition into which is incorporated a considerable amount of new material. The use of ACTH and cortisone in status asthmaticus is well covered and numerous other subjects, such as the allergenicity of cottonseed oil, are brought up to date.

The book offers a brief and simple exposition of practical methods of allergic diagnosis and treatment. The coverage of theoretical aspects is less adequate. Like many short introductory manuals of allergy, this book includes a chapter on preparation of extracts for testing and treatment. If the volume is intended for the general practitioner, as stated in the preface, it would seem more logical to devote this space to more detail of diagnosis and treatment, rather than tedious laboratory procedures which can be better performed by drug manufacturers.

On the whole, this book is a helpful guide for the general practitioner who has occasion to treat the simpler forms of allergic disease.

Clinical Allergy. A Different Approach. By Marion T. Davidson, M.D., Birmingham, 1951, American Printing Co. 175 pages, $5.00.

This book is dedicated to the thesis that in allergy there is no immunity and that in immunity there is no allergy. Since the relationship between allergy and immunity remains to be precisely defined, differences of opinion are justifiable and new evidence is most welcome. The present book presents opinions which are widely at variance with the views of most students of the subject but offers no valid proof of its statements. The beliefs that a positive tuberculin reaction represents acquired sensitization and that both human allergy and experimental anaphylaxis are related to the presence of antibodies, both of which are rejected by the author, have been based on the cumulation of many years of work by numerous competent investigators. If Dr. Davidson has sufficient evidence to outweigh this, he does not present it in the present book.

The practical portion of the book, devoted to methods of diagnosis and treatment, is more conservative in its views. Even here, however, there are statements which can only be attributed to lack of experience. In regard to molds as allergens, it is stated, "all molds and fungi tried on skin tests reacted equally or not at all. All skin test reactions were of the delayed or inflammatory type. No allergic type reactions were seen to molds or fungi." Likewise the method of passive transfer is rejected since "in the few passive transfer tests tried, the only reactions seen have been of the delayed 24-hour inflammatory type."

It is doubtful if the unsupported statements made in this book will influence the opinions of any critical reader who is acquainted with the accepted principles of allergy. As a first introduction to the subject, it can only cause confusion.

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